# MEDFACTS

POCKET GUIDE OF DRUG INTERACTIONS

Second Edition

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Bone Care

Rephrology Pharmacy Associates



This drug interactions pocket guide was written on behalf of Nephrology Pharmacy Associates, Inc. (NPA) by George R. Bailie, PharmD, PhD, Curtis A. Johnson, PharmD, Nancy A. Mason, PharmD, and Wendy L. St. Peter, PharmD, BCPS.

NPA acknowledges the assistance of Fangyan Sy, PharmD.

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# **Preface**

Patients with acute renal failure, chronic kidney disease (CKD) or those treated with dialysis or kidney transplantation are frequently prescribed numerous medications. Drugs of many therapeutic classes are used to treat the underlying diseases leading to CKD, such as diabetes mellitus and hypertension, while others are used to control or treat the common complications of CKD, such as anemia, renal bone disease and lipid disorders. Dialysis patients often are prescribed 10 to 12 medications. With such a large number of medications, there is an increased risk for drug interactions. The accompanying table has been prepared as a reference regarding the most clinically significant drug interactions that might occur, together with an indication of the possible consequence. This table should be used as a general guideline.

Sometimes information is known about one specific drug within a certain drug class, while additional information is not known about other agents within the same therapeutic category. Clinicians must be aware of this possibility and use their best judgement when prescribing or assessing drug therapy.

# **Types of Drug Interactions**

Drug interactions are often classified as either pharmacodynamic or pharmacokinetic interactions. Pharmacodynamic interactions include those that result in additive or antagonistic pharmacological effects. Pharmacokinetic interactions involve induction or inhibition of metabolizing enzymes in the liver or elsewhere, displacement of drug from plasma protein binding sites, alterations in gastrointestinal absorption, or competition for active renal secretion.

The frequency and prevalence of interactions is dependent upon the number of concomitant medications and the complexity of the regimens. The prevalence is also dependent upon other variables, such as patient adherence, hydration and nutritional status, degree of renal or hepatic impairment, smoking and alcohol use, genetics and drug dosing. Additionally, some patients may exhibit evidence of a particular drug interaction, while others with the same drug combination do not.

# Pharmacodynamic interactions

This type of interaction will not be addressed in this reference, since these should be reasonably easy to predict, knowing the pharmacology of any given drug.

### Pharmacokinetic interactions

## Interactions Resulting from Alterations in Gastrointestinal Absorption

The rate and extent of drug absorption after oral administration may be grossly altered by other agents. Absorption of a drug is a function of the drug's ability to diffuse from the lumen of the gastrointestinal tract into the systemic circulation. Changes in intestinal pH may profoundly affect drug diffusion as well as dissolution of the dosage form. For example, the absorption of ketoconazole is reduced by the co-administration of antacids or H<sub>2</sub>-blockers (e.g. ranitidine, famotidine) that reduce the extent to which the ketoconazole tablet is dissolved. Formation of insoluble complexes by a process known as chelation is another mechanism by which a drug interaction may lead to reduced oral absorption. For example, fluoroquinolones (e.g. ciprofloxacin) and divalent metal ions (such as calcium and iron) form an insoluble complex that results in reduced absorption of both the antibiotic and the metal ion. Interactions that decrease the rate of drug absorption may be of little importance, since the overall extent of absorption may remain unaltered.

# Interactions Resulting from Alterations in Metabolizing Enzymes

The liver is the major, though not exclusive, site for drug metabolism. Other sites include the kidney and the lining of the gastrointestinal tract. The two main types of hepatic drug metabolism are phase I and phase II reactions. Phase I oxidative reactions are the initial step in drug biotransformation, and are mediated by the cytochrome P-450 (CYP) system. This complex superfamily of enzymes has been subclassified into numerous enzymatic subfamilies. The most common CYP subfamilies include CYP1A2, CYP2C9, CYP2C19, CYP2D6, CYP2E1, and CYP3A4. These enzymes may be induced or inhibited by other agents, thereby leading to an increase or decrease in the metabolism of the primary drug. Phase II reactions occur following Phase I reactions. In this process, drug metabolites are converted into more water-soluble compounds that can be more easily eliminated by the kidneys.

**Enzyme induction** may result in increased CYP enzyme synthesis, faster drug metabolism, subtherapeutic drug concentrations and the risk for ineffective drug therapy. The rapidity of the enzyme induction is dependent upon the half-life of the inducing drug as well as the rate of synthesis of new enzymes. Examples of drugs that cause enzyme induction are the barbiturates, some anticonvulsants and rifampin.

**Enzyme inhibition** may result from noncompetitive or competitive inhibition of CYP enzymes by a second drug, an effect that may occur rapidly. Examples of hepatic enzyme inhibitors include cimetidine, fluconazole and erythromycin. The result of noncompetitive enzyme inhibition by addition of a second agent is slower metabolism of the first drug, higher plasma drug concentrations, and a risk for toxicity. In the case of competitive inhibition, the metabolism of both drugs can be reduced, resulting in higher than expected concentrations of each drug.

A few drugs are metabolized by enzymes found in cells lining the gastrointestinal tract. One of these drugs is cyclosporine. Some foods and other preparations such as grapefruit juice contain certain substances that may inhibit those specific enzymes, resulting in elevated serum cyclosporine concentrations.

# Interactions Resulting from Alterations in Protein Binding

Drugs may exist in plasma either reversibly bound to plasma proteins or in the free (unbound) state. The primary drug-binding plasma proteins are albumin and  $\alpha_1$ -acid glycoprotein. It is free drug that exerts the pharmacological effect. Drugs may compete with each other for plasma protein binding sites, and when this occurs, one drug may displace another that was previously bound to the protein. Displacement of a drug from its binding sites will therefore increase that agent's unbound concentrations, perhaps resulting in toxicity.

Some drugs normally exist in a state of high protein binding, often exceeding 90%. Thus, even a small decrease in protein binding could significantly increase the free concentrations. Drugs which are normally highly protein bound, and which might participate in binding interactions, include anticonvulsants and warfarin.

## Interactions Resulting from Changes in Renal Excretion

The majority of renally eliminated drugs are excreted via passive glomerular filtration. Some drugs are eliminated via active tubular secretion, such as penicillins, cephalosporins, and most diuretics. The active secretion may be inhibited by secondary agents, such as cimetidine, nonsteroidal anti-inflammatory agents and probenecid, with resulting elevations in the serum drug concentrations and reduced urinary drug concentrations. In some cases, the interaction is desirable, while others may lead to adverse therapeutic outcomes.

# Risk Factors and Management of Drug Interactions

In general, the more complex a patient's drug regimen, the higher the risk for interactions. CKD patients often take numerous medications. The average age of a dialysis patient is over 60 years and as a group, elderly patients are more prone to experience drug interactions because of reduced hepatic and renal function. Identification of the potential for interactions may enable the clinician to avoid its occurrence. Drugs that require careful dose titration to maintain efficacy and avoid toxicity must be monitored particularly carefully for drug interactions. Most drug interactions can be avoided or managed by substitution of one or more agents or more intense monitoring for the potential result. Other management strategies include separation of doses of interacting agents (e.g. ciprofloxacin and calcium) or prospective adjustment of doses.

# Clinical Significance of Interactions

This guide lists only those interactions that have been previously rated as having a moderate or high level of clinical significance by the *Drug Interaction Facts* (see References). This rating scale requires that a potential interaction has a moderate to major severity. The effects of a *moderate* interaction may cause a deterioration in the patient's clinical status, resulting in additional treatment, hospitalization, and/or an extended hospital stay. The effects of a *major* interaction are potentially life-threatening or can lead to permanent damage. In addition to being clinically significant, the interaction must be reasonably documented in the literature (suspected, probable, or established). Therefore, the accompanying table is NOT an all-inclusive list of every possible drug interaction.

# **Key to the Table**

The accompanying table contains four columns. The first is titled "Drug," and lists the primary drugs and drug classes, by generic name, which may have a significant interaction. The drugs are listed according to therapeutic classes.

The second column is titled "Interacting Drug," and lists drugs or drug classes that have potential clinically significant interactions with the primary listed drugs. These two columns are cross-referenced, as appropriate.

The third column, "Potential Effect," gives a short description of the possible clinical outcome of the interaction. The outcomes listed are possible, not definite, events. Clinicians must be aware that not all patients will manifest these interactions.

The last column, "Management," indicates suggested strategies for prevention, monitoring, and managing any potential interactions. If combination therapy of interacting drugs cannot be avoided, the patient should be advised of any potential adverse effects. Always monitor the patient for any changes in clinical response when starting, stopping, or changing the dose of interacting drugs. Also monitor for any signs/symptoms of known toxicities. Appropriate clinical intervention should be taken when necessary.

# References and Additional Reading

Further information about the listings in the table may be found in reference number 1. Additional readings are listed for the convenience of the reader.

- Tatro DS (ed). Drug Interaction Facts 2004. Facts and Comparisons, St. Louis, MO, 2004.
- 2. Stockley IH, Drug Interactions, 5th ed. London: Pharmaceutical Press; 1999.
- 3. Landrum EL. Update: clinically significant cytochrome P-450 drug interactions. *Pharmacotherapy* 1998; 18:84-112.

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT	
ANEMIA AGENTS	3			
Androgens				
Nandrolone decanoate	Warfarin, see Anticoagulants/	Thrombolytic Agents—Androgens		
Methyltestosterone/ Testosterone	Cyclosporine, see <i>Transplant</i> i	Immunosuppressants—Androgens		
	Warfarin, see Anticoagulants/	Thrombolytic Agents—Androgens		
Epoetin Alfa	No interactions noted.			
Iron Products				
Iron Salts (IV) [iron dextran, ferric gluconate, iron sucrose]	Chloramphenicol	Increased concentrations of iron.	Use alternative antibiotic if possible. Otherwise, monitor iron stores and adjust iron replacement as needed.	
Iron Salts (Oral) [ferrous fumarate, ferrous gluconate, ferrous sulfate, iron polysaccharide]	Chloramphenicol	Increased concentrations. of iron.	Use alternative antibiotic if possible. Otherwise monitor iron stores and adjust iron replacement as needed.	
	Levodopa, see <i>Antiparkinson Agents</i>			
	Levothyroxine, see Miscellaneous Agents			
	Mycophenolate mofetil, see <i>Transplant Immunosuppressants</i>			
	Penicillamine	Decreased GI absorption of penicillamine.	Administer penicillamine on an empty stomach. Separate administration times.	
	Phosphate Binders/Antacids [aluminum hydroxide, aluminum-magnesium hydroxide, calcium acetate, calcium carbonate, magnesium hydroxide]	Decreased GI absorption of iron.	Separate administration times.	
	Quinolones, see Antimicrobial Agents (Antibacterial Antibiotics)			
	Tetracyclines, see Antimicrobial Agents (Antibacterial Antibiotics)			
<b>ANTIHYPERTENS</b>	IVE AND CARDIOVA	SCULAR AGENTS		
Adrenergic Modifiers				
Clonidine	Beta-Blockers [acebutolol, atenolol, betaxolol, carteolol, esmolol, metoprolol, nadolol,	Increased blood pressure.	Monitor blood pressure when starting or stopping either drug. Discontinue	

Adrenergic Modifiers			
Clonidine	Beta-Blockers [acebutolol, atenolol, betaxolol, carteolol, esmolol, metoprolol, nadolol, penbutolol, pindolol, propranolol, timolol]	Increased blood pressure.	Monitor blood pressure when starting or stopping either drug. Discontinue either drug gradually.
	Tricyclic Antidepressants [amitriptyline, amoxapine, clomipramine, desipramine, doxepin, imipramine, nortriptyline, protriptyline, trimipramine]	Loss of blood pressure control. Increased risk of hypertensive crisis.	Avoid combination.
Methyldopa	Sympathomimetics [dobutamine, dopamine, ephedrine, epinephrine, mephentermine, metaraminol, methoxamine, norepinephrine, phenylephrine, pseudoephedrine]	Increased blood pressure.	Monitor blood pressure. Discontinue sympathomimetic or administer phentolamine if necessary.

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
Prazosin	Beta-Blockers [acebutolol, atenolol, betaxolol, bisoprolol, carteolol, esmolol, metoprolol, nadolol, penbutolol, pindolol, propranolol, sotalol, timolol]	Increased postural hypotension.	Monitor for symptoms of postural hypotension.
	Verapamil	Increased postural hypotension.	Monitor for symptoms of postural hypotension.
Angiotensin	Benazepril, Captopril, E	nalapril, Fosinopril, Lisinopr	il, Moexipril,
Converting Enzyme Inhibitors (ACEIs)	Perindopril, Quinapril, 1	randolapril	
Angiotensin Converting Enzyme Inhibitors-class	Indomethacin	Decreased effects of angiotensin converting enzyme inhibitor.	Monitor blood pressure. Discontinue indomethacin or use alternative antihypertensive.
	Lithium, see Sedative/Hypnotic (Miscellaneous Antidepressan	cs/Agents used in Psychiatry, Antide hts)	pressants
	Potassium-Sparing Diuretics [amiloride, spironolactone, triamterene]	Elevated serum potassium.	Monitor serum potassium.
Captopril (see also Angiotensin Converting Enzyme Inhibitors-class)	Food	Decreased GI absorption of captopril.	Administer captopril 1 hour before meals.
Angiotensin II Receptor Blockers (ARBs)	Candesartan, Eprosarta Valsartan	n, Irbesartan, Losartan, Olme	esartan, Telmisartan,
Angiotensin II Receptor Blockers- class	Lithium, see Sedative/Hypnotic (Miscellaneous Antidepressar	cs/Agents used in Psychiatry, Antide tts)	pressants
Beta-Blockers	Metoprolol, Nadolol]; N	utolol, Atenolol, Betaxolol, E oncardio-Selective [Carteol indolol, Propranolol, Sotalol	ol, Carvedilol,
Cardio-Selective and Noncardio-Selective Beta-Blockers-class	Barbiturates [amobarbital, aprobarbital, butabarbital, butalbital, mephobarbital, pentobarbital, phenobarbital, primidone, secobarbital]	Decreased bioavailability of beta-blocker.	Increase beta-blocker dose if necessary.
	Cimetidine	Increased concentrations of beta-blocker.	Monitor cardiovascular status. Decrease beta- blocker dose if necessary.
	Clonidine, see Antihypertensiv	e and Cardiovascular Agents (Adren	nergic Modifiers)
	Hydralazine	Increased concentrations of both drugs (metoprolol, propranolol).	Decrease dose of one or both drugs if necessary.
	NSAIDs [ibuprofen, indomethacin, naproxen, piroxicam]	Decreased effects of beta-blocker.	Use noninteracting NSAID if possible (eg, sulindac). Monitor blood pressure. Increase beta-blocker dose if necessary.
	Prazosin, see Antihypertensive	e and Cardiovascular Agents (Adrend	ergic Modifiers)

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
	Propafenone	Increased effects of beta-blocker (metoprolol, propanolol).	Monitor cardiovascular status. Decrease beta-blocker dose if necessary.
	Quinidine	Increased effects of beta- blocker (atenolol, propranolol, metoprolol, timolol).	Monitor cardiovascular status. Decrease beta-blocker dose if necessary.
	Rifamycins [rifabutin, rifampin]	Decreased effects of beta- blocker (atenolol, bisoprolol, metoprolol, propranolol).	Monitor cardiovascular status. Increase beta-blocker dose if necessary.
	Verapamil	Increased effects of both drugs.	Monitor cardiovascular status. Decrease dose of one or both drugs if necessary.
Noncardio-Selective Beta-Blockers-class		sive and Cardiovascular Agents ive and Cardiovascular Agents)	
	Ergot Alkaloids, see Miscellar	eous Agents	
	Insulin, see Hypoglycemic Age	ents	
	Prazosin, see Antihypertensiv	e and Cardiovascular Agents (Adrer	nergic Modifiers)
	Theophylline, see <i>Bronchodila</i>	itors	
Atenolol (see also Cardio-Selective and Noncardio-Selective Beta-Blockers-class)	Ampicillin	Decreased effects of atenolol.	Separate administration times. Monitor blood pressure. Increase atenolol. dose if necessary.
Carvedilol (see also Cardio-Selective and Noncardio-Selective Beta-Blockers-class)	Cyclosporine, see <i>Transplant</i> (	mmunosuppressants	
Labetalol (see also Cardio-Selective and Noncardio-Selective Beta-Blockers-class)	Inhalation Anesthetics [desflurane, enflurane, halothane, isoflurane, sevoflurane]	Excessive hypotension.	Monitor blood pressure. Use combination with caution. Halothane concentration should not exceed 3%.
Metoprolol (see also Cardio-Selective and Noncardio-Selective Beta-Blockers-class)	Lidocaine, see Antihypertensi	ve and Cardiovascular Agents (Antia	arrhythmic Agents)
	Thioamines [methimazole, propylthiouracil]	Increased effects of metoprolol.	Monitor cardiovascular status. Decrease metoprolol dose if necessary as patient becomes euthyroid. Use alternative beta-blocker (eg, atenolol, nadolol).
Nadolol (see also Cardio-Selective and Noncardio-Selective Beta-Blockers-class)	Lidocaine, see Antihypertensi	ve and Cardiovascular Agents (Antic	arrhythmic Agents)
Pindolol (see also Cardio-Selective and Noncardio-Selective Beta-Blockers-class)	Lidocaine, see Antihypertensi	ve and Cardiovascular Agents (Antia	arrhythmic Agents)
	Phenothiazines [chlorpromazine, thioridazine]	Increased effects of one or both drugs.	Decrease dose of one or both drugs if necessary.

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT	
Propranolol (see also Cardio-Selective and Noncardio-Selective Beta-Blockers-class)	Lidocaine, see Antihypertension	ve and Cardiovascular Agents (Antia	orrhythmic Agents)	
	Phenothiazines [chlorpromazine, thioridazine]	Increased effects of one or both drugs.	Decrease dose of one or both drugs if necessary.	
	Thioamines [methimazole, propylthiouracil]	Increased effects of propranolol.	Monitor cardiovascular status. Decrease propranolol dose if necessary as patient becomes euthyroid. Use alternative beta-blocker (eg, atenolol, nadolol).	
Sotalol (see also Cardio-Selective and Noncardio-Selective Beta-Blockers-class)	Quinolones [gatifloxacin, moxifloxacin, sparfloxacin]	Increased risk of cardiac arrhythmias, including torsades de pointes.	Avoid combination. Use alternative quinolones (eg, ciprofloxacin, levofloxacin).	
Calcium-Channel Blockers (CCBs)		iltiazem, Felodipine, Isradip , Nisoldipine, Verapamil	ine, Nicardipine,	
Bepridil	Digoxin, see Antihypertensive (Miscellaneous Antihypertens	and Cardiovascular Agents ive and Cardiovascular Agents)		
	Quinolones [gatifloxacin, moxifloxacin, sparfloxacin]	Increased risk of cardiac arrhythmias, including torsades de pointes.	Avoid combination. Use alternative quinolones (eg, ciprofloxacin, levofloxacin).	
	Ritonavir	Increased concentrations of bepridil.	Avoid combination.	
Diltiazem	Benzodiazepines, see Sedatives/Hypnotics/Agents used in Psychiatry (Sedatives)			
	Carbamazepine	Increased concentrations of carbamazepine.	Monitor carbamazepine concentrations. Adjust dose as needed when starting or stopping diltiazem.	
	Cyclosporine, see Transplant I	mmunosuppressants		
	HMG-CoA Reductase Inhibitor	s, see Hypolipidemic Agents		
	Moricizine	Increased concentrations of moricizine. Decreased concentrations of diltiazem.	Adjust dose of one or both drugs as needed.	
	Quinidine, see Antihypertensive and Cardiovascular Agents (Antiarrhythmic Agents)			
	Sirolimus, see Transplant Immunosuppressants			
	Tacrolimus, see Transplant Immunosuppressants			
	Theophyllines [aminophylline, oxtriphylline, theophylline]	Increased concentrations of theophylline.	Monitor theophylline concentrations. Adjust theophylline dose as needed when starting or stopping diltiazem.	
Felodipine	Barbiturates [amobarbital, aprobarbital, butabarbital, butalbital, mephobarbital, pentobarbital, phenobarbital, primidone, secobarbital]	Decreased effects of felodipine.	Monitor cardiovascular status. Increase felodipine dose if necessary.	
	Carbamazepine	Decreased effects of felodipine.	Monitor cardiovascular status. Increase felodipine dose if necessary.	

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
	Erythromycin	Increased effects of felodipine.	Monitor cardiovascular status. Decrease felodipine dose if necessary.
	Grapefruit Juice	Increased effects of felodipine.	Avoid combination.
	Hydantoins [ethotoin, fosphenytoin, mephenytoin, phenytoin]	Decreased effects of felodipine.	Monitor cardiovascular status Increase felodipine dose if necessary.
	Itraconazole	Increased effects of felodipine.	Monitor cardiovascular status Decrease felodipine dose if necessary.
Nicardipine	Cyclosporine, see <i>Transplant</i>	Immunosuppressants	
Nifedipine	Barbiturates [amobarbital, aprobarbital, butabarbital, butalbital, mephobarbital, pentobarbital, phenobarbital, primidone, secobarbital]	Decreased effects of nifedipine.	Monitor cardiovascular status. Increase nifedipine dose if necessary.
	Cimetidine	Increased effects of nifedipine.	Adjust nifedipine dose as needed when starting, stopping, or changing dose of cimetidine. Use alternative histamine H <sub>2</sub> -antagonist (eg, ranitidine).
	Rifampin	Decreased effects of nifedipine.	Monitor cardiovascular status. Adjust nifedipine dose as needed when starting or stopping rifampin.
	Tacrolimus, see Transplant Im	munosuppressants	
Nisoldipine	Grapefruit Juice	Increased effects of nisoldipine.	Avoid combination.
	Hydantoins [ethotoin, fosphenytoin, mephenytoin, phenytoin]	Decreased effects of nisoldipine.	Monitor cardiovascular status. Adjust nisoldipine dose when starting, stopping, or changing dose of hydantoin.
Verapamil		Beta-Blockers, see Antihypertensive and Cardiovascular Agents (Cardio-Selective and Noncardio-Selective Beta-Blockers)	
	Calcium Salts [calcium acetate, calcium carbonate, calcium chloride, calcium citrate, calcium glubionate, calcium gluconate, calcium glycerophosphate, calcium lactate, calcium levulinate, tricalcium phosphate]	Reverse clinical effects and toxicities of verapamil.	Monitor cardiovascular status. Calcium may be used to reverse verapamil toxicities.
	Carbamazepine, see Anticonv	rulsants	
	Cyclosporine, see <i>Transplant</i>	Immunosuppressants	
	Digoxin	Increased concentrations of digoxin.	Monitor cardiovascular status and digoxin concentrations. Decrease digoxin dose if necessary.
	Ethanol, see Miscellaneous A	gents	
	HMG-CoA Reductase Inhibito	rs, see Hypolipidemic Agents	

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT		
	Nondepolarizing Muscle Relaxants [atracurium, doxacurium, mivacurium, pancuronium, pipecuronium, tubocurarine, vecuronium]	Increased nondepolarizing muscle relaxant effects (prolonged respiratory depression).	Avoid combination if possible. Monitor respiratory function. Adjust nondepolarizing muscle relaxant dose as needed.		
	Prazosin, see Antihypertensiv	e and Cardiovascular Agents (Adren	nergic Modifiers)		
	Quinidine, see Antihypertensi	ve and Cardiovascular Agents (Antia	nrrhythmic Agents)		
	Rifampin	Decreased effects of oral verapamil.	Use intravenous verapamil or alternative drug. Adjust verapamil dose as needed when starting or stopping rifampin.		
Antiarrhythmic Agen	ts				
Amiodarone	Cyclosporine, see <i>Transplant</i>	Immunosuppressants			
	Digoxin, see Antihypertensive (Miscellaneous Antihypertens	and Cardiovascular Agents ive and Cardiovascular Agents)			
	Fentanyl	Increased risk of profound bradycardia, sinus arrest, and hypotension.	Avoid combination if possible. Otherwise, monitor hemodynamic status and manage with supportive treatment as needed.		
	Hydantoins [ethotoin, fosphenytoin, mephenytoin, phenytoin]	Increased concentrations of hydantoin. Decreased concentrations of amiodarone.	Monitor cardiovascular status and for signs/ symptoms of hydantoin toxicity. Adjust dose of one or both drugs as needed.		
	Procainamide, see Antihypertensive and Cardiovascular Agents (Antiarrhythmic Agents)				
	Protease Inhibitors [indinavir, ritonavir]	Increased concentrations of amiodarone.	Avoid combination.		
	Quinidine, see Antihypertensive and Cardiovascular Agents (Antiarrhythmic Agents)				
	Quinolones [gatifloxacin, moxifloxacin, sparfloxacin]	Increased risk of cardiac arrhythmias, including torsades de pointes.	Avoid combination. Use alternative quinolones (eg, ciprofloxacin, levofloxacin).		
	Warfarin, see Anticoagulants	Thrombolytic Agents			
Disopyramide	Hydantoins [ethotoin, fosphenytoin, mephenytoin, phenytoin]	Decreased concentrations of disopyramide. Increased risk of anticholinergic effects.	Monitor cardiovascular status and anticholinergic effects. Increase disopyramide dose if necessary.		
	Quinolones [gatifloxacin, moxifloxacin, sparfloxacin]	Increased risk of cardiac arrhythmias, including torsades de pointes.	Avoid combination. Use alternative quinolones (eg, ciprofloxacin, levofloxacin).		
	Rifampin	Decreased concentrations of disopyramide.	Monitor cardiovascular status. Increase disopyramide dose if necessary.		
Flecainide	Ritonavir	Increased concentrations of flecainide.	Avoid combination.		

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
Lidocaine	Beta-Blockers [atenolol, metoprolol, nadolol, pindolol, propranolol]	Increased concentrations of lidocaine.	Administer bolus lidocaine at a slow rate to avoid high peak concentrations and toxicity. Monitor lidocaine concentrations. Decrease lidocaine dose if necessary.
	Cimetidine	Increased concentrations of lidocaine.	Monitor lidocaine concentrations. Decrease lidocaine dose if necessary. Use alternative histamine H <sub>2</sub> -antagonist (eg, ranitidine).
Mexiletine	Hydantoins [ethotoin, fosphenytoin, mephenytoin, phenytoin]	Decreased concentrations of mexiletine.	Monitor cardiovascular status. Increase mexiletine dose if necessary.
	Theophylline, see Bronchodil	ators	
Moricizine	Cimetidine	Increased concentrations of moricizine.	Monitor ECG when starting, stopping, or changing dose of cimetidine. Decrease moricizine dose if necessary. Use alternative histamine H <sub>2</sub> - antagonist (eg, ranitidine).
Procainamide	Amiodarone	Increased concentrations of procainamide and N-acetylprocainamide.	Monitor serum procainamide and N-acetylprocainamide concentrations. Decrease procainamide dose if necessary.
	Cimetidine	Increased concentrations of procainamide and N-acetylprocainamide	Avoid combination if possible. Otherwise, decrease procainamide dose if necessary.
	Offoxacin	Increased concentrations of procainamide.	Monitor serum procainamide concentrations. Decrease procainamide dose if necessary.
	Quinolones [gatifloxacin, moxifloxacin, sparfloxacin]	Increased risk of cardiac arrhythmias, including torsades de pointes.	Avoid combination. Use alternative quinolones (eg, ciprofloxacin, levofloxacin).
	Trimethoprim	Increased concentrations of procainamide and N-acetylprocainamide.	Monitor serum procainamide and N-acetylprocainamide concentrations. Decrease procainamide dose if necessary.
Propafenone	Quinidine	Increased concentrations of propafenone.	Monitor cardiovascular status. Decrease propafenone dose or extend dosing interval if necessary.
	Ritonavir	Increased concentrations of propafenone.	Avoid combination.
Quinidine	Amiloride	Increased risk of cardiac arrhythmias and reversal of quinidine effects.	Avoid combination if possible. Otherwise, closely monitor ECG.

DRUG

INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
Amiodarone	Increased concentrations of quinidine. Increased risk of cardiac arrhythimas.	Avoid combination if possible. Otherwise, monitor quinidine concentrations and decrease quinidine dose if necessary.
Barbiturates [amobarbital, aprobarbital, butabarbital, butalbital, mephobarbital, pentobarbital, phenobarbital, primidone, secobarbital]	Decreased concentrations of quinidine	Monitor quinidine concentrations. Adjust quinidine dose as needed when starting, stopping, or changing dose of barbiturate.
Cimetidine	Increased concentrations of quinidine.	Avoid combination. if possible. Otherwise, monitor quinidine concentrations and decrease quinidine dose if necessary.
Codeine, see Pain Medication	s (Narcotic)	
Digoxin, see Antihypertensive (Miscellaneous Antihypertens	and Cardiovascular Agents ive and Cardiovascular Agents)	
Diltiazem	Increased concentrations of quinidine.	Monitor cardiovascular status and quinidine concentrations. Adjust quinidine dose as needed when starting or stopping diltiazem.
Hydantoins [fosphenytoin, phenytoin]	Decreased concentrations of quinidine.	Monitor quinidine concentrations. Increase quinidine dose if necessary.
Itraconazole	Increased concentrations of quinidine.	Monitor quinidine concentrations. Decrease quinidine dose if necessary.
Phosphate Binders/Antacids [aluminum hydroxide, aluminum-magnesium hydroxide, magnesium hydroxide, sodium bicarbonate]	Increased concentrations of quinidine.	Monitor quinidine concentrations. Decrease quinidine dose if necessary.
Propafenone, see Antihyperte	nsive and Cardiovascular Agents (A	ntiarrhythmic Agents)
Quinolones [gatifloxacin, moxifloxacin, sparfloxacin]	Increased risk of cardiac arrhythmias, including torsades de pointes.	Avoid combination. Use alternative quinolones (eg, ciprofloxacin, levofloxacin).
Rifamycins [rifabutin, rifampin]	Decreased concentrations of quinidine.	Monitor quinidine concentrations when starting, stopping, or changing dose of rifamycin. Adjust quinidine dose as needed.
Ritonavir	Increased concentrations of quinidine.	Avoid combination.

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
	Verapamil	Increased concentrations of quinidine. Increased risk of cardiac arrhythimas and hypotension.	Avoid combination if possible Otherwise, monitor cardiovascular status and quinidine concentrations. Stop one or both drugs if interaction develops and treat symptomatically.
	Warfarin, see Anticoagulants/	Thrombolytic Agents	
Nitrates	Amyl Nitrite, Isosorbide	Dinitrate, Isosorbide Mon	onitrate, Nitroglycerin
Nitrates-class	Ergot Alkaloids, see Miscellar	eous Agents	
	Phosphodiesterase-5 Enzyme Inhibitors [sildenafil, tradalafil, vardenafil]	Severe hypotension.	Avoid combination.
Nitroglycerin	Alteplase (tPA)	Decreased effects of tPA.	Avoid combination.
Miscellaneous Ar	ntihypertensive and Cardiova	scular Agents	
Digoxin	Aminoglycosides [kanamycin, neomycin, paromomycin]	Decreased concentrations of digoxin.	Monitor digoxin concentrations. Increase digoxin dose if necessary.
	Amiodarone	Increased concentrations of digoxin.	Monitor digoxin concentrations and for signs/symptoms of digoxin toxicity. Decrease digoxin dose if necessary.
	Antineoplastic Agents [bleomycin, carmustine, cyclophosphamide, cytarabine, doxorubicin, methotrexate, vincristine]	Decreased concentrations of digoxin.	Monitor digoxin concentrations. Increase digoxin dose if necessary.
	Bepridil	Increased concentrations of digoxin. Increased negative chronotropic effects.	Monitor cardiovascular status. Decrease digoxin dose if necessary.
	Cholestyramine	Decreased concentrations of digoxin.	Separate administration times. Monitor for decreased digoxin effects. Increase digoxin dose if necessary.
	Cyclosporine	Increased concentrations of digoxin.	Monitor digoxin concentrations and for signs/symptoms of digoxin toxicity. Decrease digoxin dose if necessary.
	Indomethacin	Increased concentrations of digoxin in premature infants.	Monitor digoxin concentrations and for signs/symptoms of digoxin toxicity. Decrease digoxin dose if necessary.
	Itraconazole	Increased concentrations of digoxin in premature infants.	Monitor digoxin concentrations and for signs/symptoms of digoxin toxicity. Decrease digoxin dose if necessary.

DRUG

INTERACTING DRUG

POTENTIAL EFFECT

MANAGEMENT

DKUG	INTERACTING DRUG	PUTENTIAL EFFECT	MANAGEMENT
	Loop Diuretics (bumetanide, ethacrynic acid, furosemide)	Increased risk of arrhythmias.	Monitor serum potassium and magnesium concentrations. Supplement electrolytes if necessary. Restrict dietary and sodium intake or use potassium-sparing diuretics.
	Macrolide Antibiotics [clarithromycin, erythromycin]	Increased concentrations of digoxin.	Monitor digoxin concentrations and for signs/symptoms of digoxin toxicity. Decrease digoxin dose if necessary.
	Metoclopramide	Decreased concentrations of digoxin.	Monitor for decreased digoxin effects. Increase digoxin dose if necessary.
	Penicillamine	Decreased concentrations of digoxin.	Monitor digoxin concentrations and for signs/symptoms of digoxin toxicity. Increase digoxin dose if necessary.
	Propafenone	Increased concentrations of digoxin.	Monitor digoxin concentrations and for signs/symptoms of digoxin toxicity. Decrease digoxin dose if necessary.
	Quinidine	Increased concentrations of digoxin.	Monitor digoxin concentrations and for signs/symptoms of digoxin toxicity. Decrease digoxin dose if necessary.
	Quinine	Increased concentrations of digoxin.	Monitor digoxin concentrations and for signs/symptoms of digoxin toxicity. Decrease digoxin dose if necessary.
	Spironolactone	Decreased inotropic effects.	Monitor for decreased digoxin effects. Increase digoxin dose if necessary.
	Tetracyclines [demeclocycline, doxycycline, minocycline, oxytetracycline, tetracycline]	Increased concentrations of digoxin.	Monitor digoxin concentrations and for signs/symptoms of digoxin toxicity. Decrease digoxin dose if necessary.
	Thiazide Diuretics [bendroflumethiazide, chlorothiazide, chlorothiazide, hydrochlorothiazide, hydroflumethiazide, indapamide, methyclothiazide, metolazone, polythiazide, trichlormethiazide]	Increased risk of arrhythmias.	Monitor serum potassium and magnesium concentrations. Supplement electrolytes if necessary. Restrict dietary and sodium intake or use potassium-sparing diuretics.
	Thioamines [methimazole, propylthiouracil]	Increased concentrations of digoxin.	Monitor digoxin concentrations and for signs/symptoms of digoxin toxicity. Decrease digoxin dose if necessary.

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
	Thyroid Hormones [levothyroxine, liothyronine, liotrix, thyroid]	Decreased concentrations of digoxin	Increase digoxin dose if necessary in hypothyroid patients if they become euthyroid.
	- Verapamil	Increased concentrations of digoxin	Monitor digoxin concentrations and for signs, symptoms of digoxin toxicity. Decrease digoxin dose if necessary.
Epinephrine	Beta-Blockers [carteolol, nadolol, penbutolol, pindolol, propranolol, timolol]	Initial hypertensive episode, followed by reflex bradycardia.	Avoid combination if possible Discontinue beta-blocker 3 days prior to epinephrine use if possible. Otherwise, monitor vital signs and use IV chlorpromazine, IV hydralazine, IV aminophylline and/or IV atropine if necessary.
Hydralazine	Beta-Blockers, see Antihyper (Cardio-Selective and Noncar	tensive and Cardiovascular Agents dio-Selective Beta-Blockers)	
<u>ANTIMICROBIAL</u>	AGENTS		
ANTIBACTERIAL ANT	TIBIOTICS		
Aminoglycosides	Amikacin, Gentamicin,	Kanamycin, Neomycin, Stre	ptomycin, Tobramycin
Aminoglycosides-class	Cephalosporins [cefamandole, cefazolin, cefonicid, cefoperazone, cefotaxime, cefotetan, cefoxitin, ceftazidime, ceftizoxime, ceftriaxone, cefuroxime, cephalothin, cephapirin, cephradine]	Increased risk of nephrotoxicity.	Monitor aminoglycoside concentrations and kidney function.
	Digoxin, see Antihypertensive (Miscellaneous Antihypertens	and Cardiovascular Agents ive and Cardiovascular Agents)	
	Loop Diuretics (bumetanide, ethacrynic acid, furosemide, torsemide)	Increased risk of auditory toxicity.	Avoid excessive doses of either drug. Monitor aminoglycoside concentrations. Use alternative antibiotic if possible.
	NSAIDs [diclofenac, etodolac, fenoprofen, flubiprofen, ibuprofen, indomethacin, ketoprofen, ketorolac, meclofenamate, mefenamic acid, nabumetone, naproxen, oxaprozin, piroxicam, sulindac, tolmetin]	Increased concentrations of aminoglycoside in premature infants.	Avoid combination if possible Otherwise, decrease aminoglycoside dose before starting NSAID. Monitor aminoglycoside concentrations and renal function.
	Penicillins [ampicillin, methicillin, mezlocillin, nafcillin, oxacillin, penicillin G, piperacillin, ticarcillin]	Inactivation of aminoglycoside.	Do not mix drugs in same solution. Separate administration times by at least 2 hours.

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
Cephalosporins		n, Cefonicid, Cefoperazone, Ceftizoxime, Ceftriaxone, C e	
Cephalosporins-class	Aminoglycosides, see Antimi	icrobial Agents (Antibacterial Antibi	otics)
	Warfarin, see Anticoagulants	s/Thrombolytic Agents	
<b>Cefamandol</b> (see also Cephalosporins-class)	Ethanol, see <i>Miscellaneous</i> A	Agents	
Cefonicid (see also Cephalosporins-class)	Ethanol, see Miscellaneous	Agents	
<b>Cefoperazone</b> (see also Cephalosporins-class)	Ethanol, see <i>Miscellaneous i</i>	Agents	
Ceforanide (see also Cephalosporins-class)	Ethanol, see Miscellaneous	Agents	
Cefotetan (see also Cephalosporins-class)	Ethanol, see <i>Miscellaneous</i> A	Agents	
Moxalactam (see also Cephalosporins-class)	Ethanol, see <i>Miscellaneous</i> A	Agents	
Macrolide Antibiotics	Azithromycin, Clarithro	omycin, Erythromycin, Trolea	andomycin
Macrolide Antibiotics-class	Cyclosporine, see <i>Transplant</i>	t Immunosuppressants	
	HMG-CoA Reductase Inhibit	ors, see Hypolipidemic Agents	
	Theophylline, see <i>Bronchodilators</i>		
Clarithromycin (see also Macrolide Antibiotics-class)	Buspirone, see Sedatives/Hypnotics/Agents used in Psychiatry (Miscellaneous Sed		Miscellaneous Sedatives)
	Carbamazepine, see Anticon	vulsants	
		e and Cardiovascular Agents sive and Cardiovascular Agents)—i	Macrolide Antibiotics
	Ergot Alkaloids, see <i>Miscella</i>	neous Agents— Macrolide Antibiot	ics
	Rifamycins [rifabutin, rifampin, rifapentine]	Decreased effects of clarithromycin. Increased adverse effects of rifamycin.	Monitor for increased rifamycin adverse effects and decreased response to macrolide antibiotic. Use alternative antibiotic (eg, azithromycin, dirithromycin).
	Tacrolimus, see Transplant Immunosuppressants— Macrolide Antibiotics		
	Warfarin, see Anticoagulants	s/Thrombolytic Agents—Macrolide .	Antibiotics
Erythromycin (see also Macrolide Antibiotics-class)	see also Macrolide		hiatry (Sedatives)
	Bromocriptine	Increased concentrations of bromocriptine.	Monitor for signs/symptoms of bromocriptine toxicity. Decrease bromocriptine dose if necessary.
	Buspirone, see Sedatives/Hy Macrolide Antibiotics	pnotics/Agents used in Psychiatry (	Miscellaneous Sedatives)—
	Carbamazepine, see Anticon	vulsants—Macrolide Antibiotics	

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT		
	Digoxin, see Antihypertensive Cardiovascular Agents)—Mad	and Cardiovascular Agents (Miscell crolide Antibiotics	laneous Antihypertensive and		
	Ergot Alkaloids, see Miscellaneous Agents—Macrolide Antibiotics				
	Felodipine, see Antihypertensi	ive and Cardiovascular Agents (Calc	ium-Channel Blockers)		
	Food	Decreased GI absorption of erythromycin.	Administer erythromycin stearate and non-enteric tablets at least 2 hours before or after a meal.		
	Grapefruit Juice	Increased concentrations of erythromycin.	Avoid combination.		
	Methylprednisolone, see <i>Corti</i>	icosteroids			
	Quinolones [gatifloxacin, moxifloxacin, sparfloxacin]	Increased risk of cardiac arrhythmias, including torsades de pointes.	Avoid combination. Use alternative quinolones (eg, ciprofloxacin, levofloxacin).		
	Rifamycins [rifabutin, rifampin]	Decreased effects of erythromycin Increased adverse effects of rifamycin.	Monitor for increased rifamycin adverse effects and decreased response to macrolide antibiotic. Use alternative antibiotic (eg, azithromycin, dirithromycin).		
	Tacrolimus, see Transplant Immunosuppressants—Macrolide Antibiotics				
	Warfarin, see Anticoagulants/	Thrombolytic Agents—Macrolide A	ntibiotics		
Penicillins		, Bacampicillin, Carbenicilli in, Mezlocillin, Penicillin G,			
Penicillins-class	Aminoglycosides, see Antimicrobial Agents (Antibacterial Antibiotics)				
	Food	Decreased or delayed GI absorption of oral penicillins.	Administer penicillin at least 2 hours before or after a meal.		
	Methotrexate, see Antineoplastic Agents				
	Tetracyclines [demeclocycline, doxycycline, minocycline, oxytetracycline, tetracycline]	Decreased effects of penicillins.	Avoid combination.		
	Warfarin, see Anticoagulants/	Thrombolytic Agents			
<b>Ampicillin</b> (see also Penicillins-class)	Allopurinol	Increased rate of ampicillinassociated skin rash.	Decrease allopurinol dose or use alternative drug if rash develops.		
	Atenolol	Decreased effects of atenolol.	Separate administration times. Monitor blood pressure. Increase atenolol dose if necessary.		
Quinolones		acin, Gemifloxacin, Levoflox c Acid, Norfloxacin, Ofloxac			
Quinolones-class	Didanosine	Decreased GI absorption of quinolone.	Administer didanosine at least 6 hours before or 2 hours after quinolone		

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT	
	Iron Salts (Oral) [ferrous fumarate, ferrous gluconate, ferrous sulfate, iron polysaccharide]	Decreased GI absorption of quinolone.	Avoid combination.	
	Phosphate Binders/Antacids [aluminum hydroxide, aluminum-magnesium hydroxide, calcium acetate, calcium carbonate, magnesium hydroxide]	Decreased GI absorption of quinolone.	Separate administration times by at least 2 hours.	
	Sucralfate	Decreased GI absorption of quinolone.	Administer sucralfate at least 6 hours after quinolone.	
Ciprofloxacin (see also Quinolones-class)	Cyclosporine, see <i>Transplant</i>	lmmunosuppressants—Quinolones		
	Food [milk]	Decreased GI absorption of ciprofloxacin.	Avoid combination.	
	Theophylline, see Bronchodila	ntors—Quinolones		
Norfloxacin (see also Quinolones-class)	Cyclosporine, see <i>Transplant</i> i	lmmunosuppressants—Quinolones		
	Food [milk]	Decreased GI absorption of norfloxacin.	Avoid combination.	
	Theophylline, see <i>Bronchodila</i>	ntors—Quinolones		
Ofloxacin (see also Quinolones-class)	Procainamide, see Antihypertensive and Cardiovascular Agents (Antiarrhythmic Agents)			
Sparfloxacin (see also Quinolones-class)	Amiodarone, see Antihyperter	nsive and Cardiovascular Agents (Ar	ntiarrhythmic Agents)	
	Bepridil	Increased risk of cardiac arrhythmias, including torsades de pointes.	Avoid combination.	
	Disopyramide, see Antihypertensive and Cardiovascular Agents (Antiarrhythmic Agents)			
	Erythromycin, see Antimicrob	ial Agents, Antibacterial Antibiotics	(Macrolide Antibiotics)	
	Phenothiazines, see <i>Sedatives</i>	s/Hypnotics/Agents used in Psychia	try (Antipsychotic Agents)	
	Procainamide, see Antihypert	ensive and Cardiovascular Agents (	Antiarrhythmic Agents)	
	Quinidine, see Antihypertensi	ve and Cardiovascular Agents (Antia	nrrhythmic Agents)	
	Sotalol, see Antihypertensive	and Cardiovascular Agents (Beta-Bi	lockers)	
	Tricyclic Antidepressants, see (Tricyclic Antidepressants)	Sedatives/Hypnotics/Agents used i	in Psychiatry	
Tetracyclines	Demeclocycline, Doxyc Oxytetracycline, Tetrac	cycline, Methacycline, Mino ycline	cycline,	
Tetracyclines-class	Bismuth Salts [bismuth subgallate, bismuth subsalicylate]	Decreased GI absorption of tetracycline.	Separate administration times by at least 2 hours.	
	Iron Salts (Oral) [ferrous fumarate, ferrous gluconate, ferrous sulfate, iron polysaccharide]	Decreased GI absorption of tetracycline.	Separate administration times by at least 3-4 hours. Use enteric-coated or sustained-release formulation of iron salt.	

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
	Phosphate Binders/Antacids (aluminum carbonate, aluminum hydroxide, calcium acetate, calcium carbonate, calcium gluconate, calcium gluconate, calcium gluconate, calcium gluconate, calcium gluconate, magnesium carbonate, magnesium gluconate, magnesium hydroxide, magnesium oxide, magnesium sulfate, magnesium trisilicate)	Decreased GI absorption of tetracycline.	Separate administration times by at least 3-4 hours.
	Urinary Alkalinizers [potassium citrate, sodium acetate, sodium bicarbonate, sodium citrate, sodium lactate, tromethamine]	Decreased concentrations of tetracycline.	Separate administration times by at least 3-4 hours. Increase tetracycline dose if necessary.
	Zinc Salts [zinc gluconate, zinc sulfate]	Decreased GI absorption of tetracycline.	Separate administration times by at least 3-4 hours.
Doxycycline (see also Tetracyclines-class)	Barbiturates (amobarbital, aprobarbital, butabarbital, butalbital, mephobarbital, metharbital, pentobarbital, phenobarbital, primidone, secobarbital]	Decreased concentrations of doxycycline.	Increase doxycycline dose if necessary. Use alternative tetracycline.
	Carbamazepine	Decreased concentrations of doxycycline.	Increase doxycycline dose if necessary. Use alternative tetracycline.
	Digoxin, see Antihypertensive and Cardiovascular Agents (Miscellaneous Antihypertensive and Cardiovascular Agents)—Tetracyclines		
	Hydantoins [ethotoin, fosphenytoin, phenytoin]	Decreased concentrations of doxycycline.	Increase doxycycline dose if necessary. Use alternative tetracycline.
	Penicillins, see Antimicrobial	Agents (Antibacterial Antibiotics)—	Tetracyclines
	Rifamycins [rifabutin, rifampin]	Decreased concentrations of doxycycline.	Increase doxycycline dose if necessary. Use alternative tetracycline.
Minocycline (see also Tetracyclines-class)	Digoxin, see Antihypertensive (Miscellaneous Antihypertens	and Cardiovascular Agents ive and Cardiovascular Agents)—T	etracyclines
	Penicillins, see Antimicrobial	Agents (Antibacterial Antibiotics)—	Tetracyclines
<b>Tetracycline</b> (see also Tetracyclines-class)	Penicillins, see Antimicrobial	Agents (Antibacterial Antibiotics)—	Tetracyclines
Miscellaneous Antib	acterial Antibiotics		
Chloramphenicol	Iron Products, see <i>Anemia Ag</i>	ents	
	Phenytoin, see Anticonvulsan	ts (Hydantoins)	
	Sulfonylureas, see <i>Hypoglyce</i>	mic Agents	
	Warfarin, see Anticoagulants/	Thrombolytic Agents	

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
Clindamycin	Aluminum Salts [aluminum carbonate, aluminum hydroxide, aluminum phosphate, attapulgite, kaolin, magaldrate]	Delayed GI absorption of clindamycin.	Administer aluminum salts at least 2 hours before clindamycin.
Dapsone	Trimethoprim	Increased concentrations of both drugs.	Monitor for methemoglobinemia.
Imipenem/Cilastatin	Cyclosporine, see <i>Transplant</i> i	lmmunosuppressants	
Metronidazole	Barbiturates [amobarbital, aprobarbital, butabarbital, butalbital, mephobarbital, pentobarbital, phenobarbital, primidone, secobarbital]	Therapeutic failure of metronidazole.	Monitor for metronidazole treatment failure. Increase metronidazole dose if necessary. Use higher initial metronidazole dose.
	Disulfiram	Acute psychosis or confusion.	Avoid combination.
	Ethanol, see Miscellaneous A	gents	
	Warfarin, see Anticoagulants/	Thrombolytic Agents	
Trimethoprim/ Sulfamethoxazole	Cyclosporine, see <i>Transplant</i>	lant Immunosuppressants—Sulfonamides	
	Dapsone, see Antimicrobial A	gents (Miscellaneous Antibacterial A	Antibiotics)
	Methotrexate, see Antineoplastic Agents—Sulfonamides		
	Phenytoin, see Anticonvulsants—Sulfonamides		
	Procainamide, see Antihypertensive and Cardiovascular Agents (Antiarrhythmic Agents)		
	Sulfonylureas, see Hypoglycemic Agents		
	Warfarin, see Anticoagulants/Thrombolytic Agents—Sulfonamides		
Vancomycin	Nondepolarizing Muscle Relaxants [atracurium, gallamine triethiodide, metocurine iodide, pancuronium, pipecuronium, tubocurarine, vecuronium]	Increased effects of nondepolarizing muscle relaxant (prolonged respiratory depression).	Avoid combination if possible. Otherwise, monitor respiratory function and adjust nondepolarizing muscle relaxant dose as needed.
Azole Antifungals	Fluconazole, Itraconazo	ole, Ketoconazole, Miconazo	le, Voriconazole
Azole Antifungals-class	Benzodiazepines, see <i>Sedativ</i>	es/Hypnotics/Agents used in Psychi	atry (Sedatives)
	Buspirone, see Sedatives/Hyp	notics/Agents used in Psychiatry (M	liscellaneous Sedatives)
	Cyclosporine, see <i>Transplant</i> i	lmmunosuppressants	
	Dexamethasone, see <i>Corticos</i>	teroids	
	Grapefruit Juice	Decreased GI absorption of azole antifungal.	Avoid combination.
	Haloperidol, see Sedatives/Hypnotics/Agents used in Psychiatry (Antipsychotic Agents)		
	HMG-CoA Reductase Inhibitors, see Hypolipidemic Agents		
	Indinavir, see Antimicrobial Ag	gents (Antiviral Agents)	
	Methylprednisolone, see <i>Cort</i>	icosteroids	
	Nelfinavir, see Antimicrobial A	Agents (Antiviral Agents)	
	Prednisolone and Prednisone,	see Corticosteroids	
	Rifamycins [rifabutin, rifampin]	Decreased concentrations of azole antifungal.	Avoid combination if possible. Otherwise, increase azole antifungal dose if necessary.

	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
	Ritonavir, see Antimicrobial Ag	gents (Antiviral Agents)	
	Saquinavir, see Antimicrobial	Agents (Antiviral Agents)	
	Tacrolimus, see <i>Transplant Imi</i>	munosuppressants	
	Warfarin, see Anticoagulants/	Thrombolytic Agents	
<b>Fluconazole</b> (see also Azole Antifungals-class)	Glimepride, see Hypoglycemic	Agents (Sulfonylureas)	
	Phenytoin, see Anticonvulsant	's	
	Tolbutamide, see <i>Hypoglycem</i>	ic Agents (Sulfonylureas)	
Itraconazole (see also Azole Antifungals-class)	Didanosine	Decreased GI absorption of itraconazole.	Separate administration by at least 2 hours.
	Digoxin, see Antihypertensive Cardiovascular Agents)	and Cardiovascular Agents (Misce	llaneous Antihypertensive and
	Felodipine, see Antihypertensi	ve and Cardiovascular Agents (Cal	cium-Channel Blockers)
	Food/Cola	Increased GI absorption of itraconazole.	Administer drug immediately after meals.
	Hydantoins [ethotoin, fosphenytoin, mephenytoin, phenytoin]	Decreased effects of itraconazole. Increased effects of hydantoin.	Avoid combination.
	Proton Pump Inhibitors [esomeprazole, lansoprazole, omeprazole, pantoprazole, rabeprazole]	Decreased GI absorption of itraconazole.	Avoid combination if possible Otherwise, administer itraconazole with an acidic beverage (cola).
	Quinidine, see Antihypertensive and Cardiovascular Agents (Antiarrhythmia Agents)		
Ketoconazole (see also Azole Antifungals-class)	Didanosine	Decreased GI absorption of ketoconazole.	Separate administration by at least 2 hours.
Histamine [cimetidin	Histamine H <sub>2</sub> -Antagonists [cimetidine, famotidine, nizatidine, ranitidine]	Decreased GI absorption of ketoconazole.	Avoid combination if possible Otherwise, administer glutamic acid hydrochloride 680 mg 15 minutes before ketoconazole.
	Hydantoins [ethotoin, fosphenytoin, mephenytoin, phenytoin]	Decreased effects of ketoconazole.	Avoid combination.
	Indinavir, see Antimicrobial Ag	gents (Antiviral Agents)	
	Proton Pump Inhibitors [esomeprazole, lansoprazole, omeprazole, pantoprazole, rabeprazole]	Decreased GI absorption of itraconazole (ketoconazole).	Avoid combination if possible Otherwise, administer ketoconazole with an acidic beverage (cola).
Voriconazole (see also Azole Antifungals-class)	Barbiturates [mephobarbital, phenobarbital]	Decreased concentrations of voriconazole.	Avoid combination.
	Carbamazepine	Decreased concentrations of voriconazole.	Avoid combination.
	Ergot Alkaloids, see Miscellan	eous Agents	
	Pimozide	Increased risk of cardiac arrhythmias, including torsades de pointes.	Avoid combination.

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT	
	Quinidine	Increased risk of cardiac arrhythmias, including torsades de pointes.	Avoid combination.	
Miscellaneous Antif	fungal Agents			
Griseofulvin	Barbiturates [amobarbital, aprobarbital, butabarbital, butalbital, mephobarbital, pentobarbital, phenobarbital, primidone, secobarbital]	Decreased concentrations of griseofulvin	Separate administration times. Increase griseofulvin dose if necessary.	
	Warfarin, see Anticoagulants	Thrombolytic Agents		
Caspofungin	Cyclosporine, see <i>Transplant</i>	lmmunosuppressants		
	Tacrolimus, see <i>Transplant Im</i>	munosuppressants		
ANTIMYCOBACTER	IAL AGENTS			
Aminosalicylic acid (PAS)	Rifampin, see Antimicrobial A	gents (Rifamycins)—Rifampin		
Isoniazid	Carbamazepine, see Anticonv	ulsants		
	Phenytoin, see Anticonvulsan	ts (Hydantoins)		
	Rifampin	Increased risk of hepatotoxicity.	Monitor liver function tests. Discontinue one or both drugs if necessary.	
Rifamycins	Rifabutin, Rifampin, Rifapentine			
Rifamycins-class	Azole Antifungals, see Antimicrobial Agents (Azole Antifungals)			
,	Bisoprolol	Decreased effects of bisoprolol.	Monitor cardiovascular status. Increase bisoprolol dose if necessary.	
	Buspirone, see Sedatives/Hyp	notics/Agents used in Psychiatry (M	liscellaneous Sedatives)	
	Clarithromycin, see Antimicro	Clarithromycin, see Antimicrobial Agents, Antibacterial Antibiotics (Macrolide Antibiotics)		
	Corticosteroids , see Corticos	teroids		
	Cyclosporine, see <i>Transplant</i>	Immunosuppressants		
	Delavirdine, see Antimicrobia	Agents (Antiviral Agents)		
	Doxycycline, see Antimicrobia	al Agents, Antibacterial Antibiotics (1	Tetracyclines)	
	Erythromycin, see Antimicrob	ial Agents, Antibacterial Antibiotics (	(Macrolide Antibiotics)	
	Estrogens, see Miscellaneous	Agents		
	Haloperidol, see Sedatives/Hypnotics/Agents used in Psychiatry (Antipsychotic Agents)			
	HMG-CoA Reductase Inhibitors, see Hypolipidemic Agents			
	Indinavir, see Antimicrobial A	Indinavir, see Antimicrobial Agents (Antiviral Agents)		
	Methadone, see Pain Medica	tions (Narcotic)		
	Metoprolol	Decreased effects of metoprolol.	Monitor cardiovascular status. Increase metoprolol dose if necessary.	
	Morphine, see Pain Medication	ons (Narcotic)		
	Nelfinavir, see Antimicrobial A	Agents (Antiviral Agents)		
	Phenytoin, see Anticonvulsan	ts (Hydantoins)		

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
	Propranolol	Decreased effects of propranolol.	Monitor cardiovascular status. Increase propranolol dose if necessary.
	Quinidine, see Antihypertensive and Cardiovascular Agents (Antial		rrhythmic Agents)
	Quinine, see Miscellaneous A	gents	
	Ritonavir, see Antimicrobial A	Ritonavir, see Antimicrobial Agents (Antiviral Agents)	
	Sulfonylureas, see <i>Hypoglyce</i>	mic Agents	
	Tacrolimus, see <i>Transplant Im</i>	munosuppressants	
	Theophyllines, see <i>Bronchodi</i>	lators	
	Tricyclic Antidepressants, see	Sedatives/Hypnotics/Agents used in	n Psychiatry (Antidepressants)
	Warfarin, see Anticoagulants/	Thrombolytic Agents	
Rifampin (see also Rifamycins-class)	Disopyramide, see Antihypert	ensive and Cardiovascular Agents (A	Antiarrhythmic Agents)
	Isoniazid, see Antimicrobial A	gents (Antimycobacterial Agents)	
	Nifedipine, see Antihypertens	ive and Cardiovascular Agents (Calc	ium-Channel Blockers)
	Verapamil, see Antihypertensi	ive and Cardiovascular Agents (Calc	ium-Channel Blockers)
ANTIVIRAL AGENTS			
Acyclovir	Thombyllines see Branchedi	latore	
Delavirdine	Theophyllines, see Bronchodilators  Ergot Alkaloids, see Miscellaneous Agents-NNRT Inhibitors		
Delavituille	Rifamycins [rifabutin, rifampin]	Decreased concentrations of delayirdine.	Avoid combination.
Didanosine	Food	Decreased GI absorption of didanosine.	Administer didanosine on an empty stomach.
	Indinavir, see Antimicrobial Agents (Antiviral Agents)		
	Itraconazole, see Antimicrobia	al Agents (Azole Antifungals)	
	Ketoconazole, see Antimicrob	ial Agents (Azole Antifungals)	
	Quinolones, see Antimicrobial	Agents (Antibacterial Antibiotics)	
Foscarnet	Cyclosporine	Increased risk of renal failure.	Avoid combination if possible Otherwise, monitor renal function and discontinue foscarnet if necessary.
Ganciclovir	Zidovudine	Increased risk of life-threatening hematologic toxicity.	Avoid combination. Use foscarnet instead.
Indinavir	Azole Antifungals [fluconazole, itraconazole, ketoconazole]	Increased concentrations of protease inhibitor.	Decrease protease inhibitor dose if necessary.
	Benzodiazepines, see <i>Sedativ Inhibitor</i>	es/Hypnotics/Agents used in Psychi	atry (Sedatives)-Protease
	Didanosine	Decreased GI absorption of indinavir.	Separate administration times by at least 1 hour on an empty stomach.
	Ergot Alkaloids, see <i>Miscellar</i>	eous Agents-Protease Inhibitors	
	Methadone, see Pain Medica	tions (Narcotic)-Protease Inhibitors	
	Rifamycins [rifabutin, rifampin, rifapentine]	Decreased concentrations of in dinavir. Increased concentrations of rifamycin.	Avoid combination if possible Otherwise, decrease rifabution dose by 50%. Increase indinvair dose if necessary.

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT		
Nelfinavir	Azole Antifungals [fluconazole, itraconazole, ketoconazole]	Increased concentrations of protease inhibitor.	Decrease protease inhibitor dose if necessary.		
	Ergot Alkaloids, see <i>Miscella</i>	neous Agents-Protease Inhibitors			
	Ethinyl Estradiol	Loss of contraceptive efficacy of ethinyl estradiol.	Use alternative nonhormonal or additional method of contraception. Use alternative protease inhibitor (eg, indinavir).		
	Methadone, see Pain Medica	tions (Narcotic)-Protease Inhibitors			
	Rifamycins [rifabutin, rifampin]	Decreased concentrations of nelfinavir.	Avoid combination if possible. Otherwise, decrease rifabutin dose by 50%. Increase nelfinavir dose if necessary.		
Ritonavir	Amiodarone, see Antihyperte	nsive and Cardiovascular Agents (Ar	ntiarrhythmic Agents)		
	Azole Antifungals [fluconazole, itraconazole, ketoconazole]	Increased concentrations of protease inhibitor.	Decrease protease inhibitor dose if necessary.		
	Benzodiazepines, see <i>Sedativ Inhibitor</i>	ves/Hypnotics/Agents used in Psychi	atry (Sedatives)-Protease		
	Buproprion, see Sedatives/Hypnotics/Agents used in Psychiatry, Antidepressants (Miscellaneous Antidepressants)				
	Clozapine, see Sedatives/Hyp	Clozapine, see Sedatives/Hypnotics/Agents used in Psychiatry (Antipsychotic Agents)			
	Encainide 	Increased concentrations of encainide.	Avoid combination.		
	Ergot Alkaloids, see Miscella	Ergot Alkaloids, see Miscellaneous Agents-Protease Inhibitors			
	Ethinyl Estradiol	Loss of contraceptive efficacy of ethinyl estradiol.	Use alternative nonhormonal or additional method of contraception. Use alternative protease inhibitor (eg, indinavir).		
	Flecainide	Increased concentrations of flecainide.	Avoid combination.		
	Meperidine, see Pain Medica	ntions (Narcotic)			
	Piroxicam, see Arthritis and G	Gout Agents (NSAIDs)			
	Propafenone	Increased concentrations of propafenone.	Avoid combination.		
	Propoxyphene, see Pain Med	lications (Narcotic)			
	Quinidine	Increased concentrations of quinidine.	Avoid combination.		
	Rifamycins [rifabutin, rifampin]	Decreased concentrations of ritonavir. Increased concentrations of rifabutin.	Avoid combination if possible Otherwise, decrease rifabutin dose by 50%. Increase ritonavir dose if necessary.		
Saquinavir	Benzodiazepines, see <i>Sedati</i> Inhibitor	ves/Hypnotics/Agents used in Psychi	atry (Sedatives)-Protease		
	Ergot Alkaloids, see Miscella	neous Agents-Protease Inhibitors			
	Grapefruit Juice	Increased concentrations of saquinavir.	Avoid combination.		

Atovaquone  Ganciclovir, see Antimicrobia. Probenecid  TS/THROMBOLYTIC Antimicroby Nitroglycerin, see Antihyperte	Rash, malaise, myalgia, and fever.	Monitor for signs/symptoms of toxicity. Decrease zidovudine dose if necessary.  Monitor for signs/symptoms
Probenecid  TS/THROMBOLYTIC A  Nitroglycerin, see Antihyperte	Rash, malaise, myalgia, and fever.	
TS/THROMBOLYTIC A	and fever.	
Nitroglycerin, see Antihyperte	AGENTS	of toxicity.
Adenosine		
	Increased effects of adenosine (profound bradycardia).	No special precautions needed when using adenosine to terminate SVT due to its short half-life. Decrease initial infusion rate of adenosine when using it to simulate exercise during cardiac imaging.
Salicylates [aspirin]	Increased risk of bleeding.	Monitor for signs/symptoms of bleeding. Treat symptomatically.
Phenytoin, see Anticonvulsan	ts	
Theophylline, see <i>Bronchodila</i>	ators	
Acetaminophen	Increased effects of warfarin.	Limit acetaminophen use. Monitor INR more frequently with chronic or high doses of acetaminophen.
Aminoglutethimide	Decreased effects of warfarin.	Monitor INR. Adjust warfarin dose as needed when starting or stopping aminoglutethimide.
Amiodarone	Increased effects of warfarin.	Monitor INR. Decrease warfarin dose empirically and adjust warfarin dose as needed.
Androgens [danazol, fluoxymesterone, methyltestosterone, nandrolone decanoate, oxandrolone, oxymetholone, stanozolol, testosterone]	Increased effects of warfarin.	Avoid combination if possible Otherwise, monitor INR and decrease warfarin dose if necessary.
Azole Antifungals [fluconazole, itraconazole, ketoconazole, miconazole]	Increased effects of warfarin.	Monitor INR. Adjust warfarin dose as needed when starting or stopping azole antifungal.
Barbiturates (amobarbital, aprobarbital, butabarbital, butalbital, mephobarbital, pentobarbital, phenobarbital, primidone, secobarbital,	Decreased effects of warfarin.	Monitor INR. Adjust warfarin dose as needed when starting or stopping barbiturate. Use benzodiazepine instead.
Carbamazepine	Decreased effects of warfarin.	Monitor INR. Adjust warfarin dose as needed when starting or stopping carbamazepine.
	Phenytoin, see Anticonvulsan Theophylline, see Bronchodila Acetaminophen  Aminoglutethimide  Amiodarone  Androgens [danazol, fluoxymesterone, methyltestosterone, nandrolone decanoate, oxandrolone, oxymetholone, stanozolol, testosterone]  Azole Antifungals [fluconazole, itraconazole, ketoconazole, miconazole]  Barbiturates [amobarbital, aprobarbital, butabarbital, pentobarbital, phenobarbital, primidone, secobarbital,	Salicylates [aspirin] Increased risk of bleeding.  Phenytoin, see Anticonvulsants Theophylline, see Bronchodilators  Acetaminophen Increased effects of warfarin.  Aminoglutethimide Decreased effects of warfarin.  Amiodarone Increased effects of warfarin.  Androgens [danazol, fluoxymesterone, methyltestosterone, nandrolone decanoate, oxandrolone, oxymetholone, stanozolol, testosterone]  Azole Antifungals [fluconazole, itraconazole, ketoconazole, miconazole] Increased effects of warfarin.  Barbiturates [amobarbital, putabarbital, butabital, mephobarbital, pentobarbital, phenobarbital, primidone, secobarbital,

DRUG

INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
Cephalosporins [cefamandole, cefazolin, cefoperazone, cefotetan, cefoxitin, ceftriaxone]	Increased effects of warfarin.	Monitor INR . Adjust warfarin dose as needed when starting or stopping cephalosporin.
Chloramphenicol	Increased effects of warfarin.	Monitor INR. Decrease warfarin dose if necessary.
Cholestyramine	Decreased effects of warfarin.	Separate administration times by at least 3 hours. Monitor INR. Increase warfarin dose if necessary.
Cimetidine	Increased effects of warfarin.	Avoid combination if possible. Otherwise, monitor INR and decrease warfarin dose if necessary. Use alternative histamine H <sub>2</sub> -antagonist (eg, ranitidine).
Dextrothyroxine	Increased effects of warfarin.	Monitor INR. Decrease warfarin dose if necessary.
Disulfiram	Increased effects of warfarin.	Monitor INR. Decrease warfarin dose if necessary.
Ethchlorvynol	Decreased effects of warfarin.	Monitor INR. Increase warfarin dose if necessary. Use benzodiazepine instead.
Fibric Acids [clofibrate, fenofibrate, gemfibrozil]	Increased effects of warfarin.	Avoid combination.
Glucagon	Increased effects of warfarin with prolonged glucagon dosing.	Monitor INR. Decrease warfarin dose if necessary.
Glutethimide	Decreased effects of warfarin.	Monitor INR. Adjust warfarin dose as needed when starting or stopping glutethimide. Use benzodiazepine instead.
Griseofulvin	Decreased effects of warfarin.	Monitor INR. Adjust warfarin dose as needed when starting, stopping, or changing dose of griseofulvin.
HMG-CoA Reductase Inhibitors [fluvastatin, lovastatin, simvastatin]	Increased effects of warfarin.	Monitor INR. Adjust warfarin dose as needed when starting or stopping HMG- CoA reductase inhibitor.
Levamisole	Increased effects of warfarin.	Monitor INR when starting or stopping levamisole. Adjust warfarin dose as needed.
Macrolide Antibiotics [azithromycin, clarithromycin, erythromycin]	Increased effects of warfarin.	Monitor INR. Decrease warfarin dose if necessary.
Metronidazole	Increased effects of warfarin.	Monitor INR. Decrease warfarin dose if necessary.
Nalidixic Acid	Increased effects of warfarin.	Monitor INR. Decrease warfarin dose if necessary.

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
	NSAIDs [diclofenac, etodolac, fenoprofen, flurbiprofen, ibuprofen, indomethacin, ketoprofen, ketorolac, meclofenamate, nabumetone, naproxen, oxaprozin, piroxicam, sulindac, tolmetin]	Increased effects of warfarin. Increased risk of bleeding.	Monitor INR and for signs/ symptoms of bleeding. Treat symptomatically.
	Penicillins (ampicillin, dicloxacillin, methicillin, mezlocillin, nafcillin, oxacillin, penicillin G, piperacillin, ticarcillin]	Increased effects of warfarin with large doses of IV penicillin. Nafcillin and dicloxacillin can cause warfarin resistance.	Monitor INR. Decrease warfarin dose if necessary.
	Quinine Derivatives [quinidine, quinine]	Increased effects of warfarin.	Monitor INR. Decrease warfarin dose if necessary.
	Rifamycins [rifabutin, rifampin, rifapentine]	Decreased effects of warfarin.	Monitor INR. Adjust warfarin dose as needed when starting or stopping rifamycin.
	Salicylates [aspirin, methylsalicylate]	Increased effects of warfarin with large doses of salicylate. Increased risk of bleeding with any aspirin dose.	Avoid large doses of aspirin. Monitor INR and for signs/symptoms of bleeding. Treat symptomatically.
	Sulfinpyrazone	Increased effects of warfarin.	Monitor INR. Decrease warfarin dose if necessary.
	Sulfonamides [sulfamethizole, sulfamethoxazole, sulfasalazine, sulfisoxazole, trimethoprim/ sulfamethoxazole]	Increased effects of warfarin.	Monitor INR. Decrease warfarin dose if necessary.
	Thioamines [methimazole, propylthiouracil]	Various effects on warfarin activity.	Monitor INR. Adjust warfarin dose as needed.
	Thyroid Hormones [levothyroxine, liothyronine, liotrix, thyroid]	Increased effects of warfarin.	Monitor INR. Adjust warfarin dose as needed when starting, stopping, or changing dose of thyroid hormone.
	Vitamin E (Tocopherol)	Increased effects of warfarin.	Monitor INR. Decrease warfarin dose if necessary.
	Vitamin K (Phytonadione)	Decreased or reversed effects of warfarin.	Avoid or minimize intake of foods with high vitamin K. Monitor INR. Adjust warfarin dose as needed.
<u>ANTICONVULS</u>			
Carbamazepine		onotics/Agents used in Psychiatry (I	· · · · · · · · · · · · · · · · · · ·
	Cimatidina	In avacand a an anniversions	A

Carbamazepine Bupropio	on, see Seaatives/Hypnotics/Agents used in Psychiatry (	•

Cimetidine	Increased concentrations of carbamazepine.	Avoid combination if possible. Otherwise, monitor carbamazepine concentrations. Decrease dose if necessary. Use alternative histamine H <sub>2</sub> -antagonist (eg, ranitidine).

Cyclosporine, see Transplant Immunosuppressants

DRUG

Dittiazem Increased concentrations of carbamazepine.  Dittiazem Increased concentrations of carbamazepine.  Doxycycline, see Antimicrobial Agents, Antibacterial Antibiotics (Tetracyclines) Felodipine, see Antimypertensive and Cardiovascular Agents (Calcium-Channel Blocke Fluoxetine Increased concentrations of carbamazepine.  Fluoxetine Increased concentrations of carbamazepine.  Grapefruit Juice Increased concentrations of carbamazepine of carbamazepine doi if necessary.  Grapefruit Juice Increased concentrations of carbamazepine of carbamazepine doi if necessary.  Grapefruit Juice Increased rose of rearbamazepine of carbamazepine doi if necessary.  Grapefruit Juice Increased rose of rearbamazepine of carbamazepine doi if necessary.  Haloperidol, see Sedatives/Hypnotics/Agents used in Psychiatry (Antipsychotic Agents of Carbamazepine doi if necessary.  Lamotrigine, see Anticonvulsants  Lithium, see Sedative/Hypnotics/Agents used in Psychiatry, Antidepressants (Miscellaneous Antidepressants)  Macrolide Antibiotics Increased concentrations of carbamazepine.  Macrolide Antibiotics Increased concentrations of carbamazepine.  Increased risk of severe adverse effects (hyperpyrexia, hyperexictability, muscle rigidity, seizures).  Nefazodone Increased concentrations of carbamazepine.  Phenytoin, see Anticonvulsants (Hydantoins)  Primidone Decreased concentrations of carbamazepine, primidone, and phenobarbital (metabolite of primidone).  Propoxyphene Increased concentrations of carbamazepine, primidone, and phenobarbital (metabolite of primidone).  Propoxyphene Increased concentrations of carbamazepine.	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
Of carbamazepine.  concentrations. Doxacycycline, see Antimicrobial Agents, Antibacterial Antibiotics (Tetracyclines)  Felodipine, see Antihypertensive and Cardiovascular Agents (Calcium-Channel Blocke Fluoxetine  Increased concentrations of carbamazepine.  Grapefruit Juice  Increased concentrations of carbamazepine do if necessary.  Grapefruit Juice  Increased concentrations of carbamazepine do if necessary.  Grapefruit Juice  Increased concentrations of carbamazepine do if necessary.  Increased risk of carbamazepine toxicity and isoniazid hepatotoxicity.  Increased risk of carbamazepine toxicity and isoniazid hepatotoxicity.  Lamotrigine, see Anticonvulsants  Lithium, see Sedative/Hypnotics/Agents used in Psychiatry, Antidepressants  Macrolide Antibiotics Increased concentrations of carbamazepine.  Increased risk of severe advised fine patients of carbamazepine.  MAO Inhibitors Isoniazid Increased risk of severe adverse effects (hyperpyrexia, hyperexcitability, muscle rigidity, seizures).  Nefazodone  Increased concentrations of carbamazepine.  Decreased concentrations of carbamazepine.  Decreased concentrations of carbamazepine.  Phenytoin, see Anticonvulsants (Hydantoins)  Primidone  Decreased concentrations of carbamazepine, primidone, and phenobarbital (metabolite of primidone).  Increased concentrations of carbamazepine, primidone concentrations of carbamazepine, primidone concentrations of carbamazepine.  Propoxyphene  Increased concentrations of carbamazepine, primidone, and phenobarbital (metabolite of primidone).  Avoid combination of possible. Otherw monitor carbamaze concentrations of carbamazepine.  Propoxyphene  Increased concentrations of carbamazepine.  Avoid combination of possible. Otherw monitor carbamaze concentrations and concentrations and carbamazepine.	Danazol		Avoid combination if possible. Otherwise, monitor carbamazepine concentrations. Decrease dose if necessary.
Felodipine, see Antihypertensive and Cardiovascular Agents (Calcium-Channel Blocker Fluoxetine Increased concentrations of carbamazepine.  Grapefruit Juice Increased concentrations of carbamazepine.  Haloperidol, see Sedatives/Hypnotics/Agents used in Psychiatry (Antipsychotic Agents and isoniazid Increased risk of carbamazepine toxicity and isoniazid hepatotoxicity.  Lamotrigine, see Anticonvulsants  Lithium, see Sedative/Hypnotics/Agents used in Psychiatry, Antidepressants  (Miscellaneous Antidepressants)  Macrolide Antibiotics Increased concentrations of carbamazepine.  MAO Inhibitors Isoniazid, phenelzine, tranylcypromine] Increased concentrations of carbamazepine.  MAO Inhibitors Increased risk of severe adverse effects (hyperpyrexia, hyperexcitability, muscle rigidity, seizures).  Nefazodone Increased concentrations of carbamazepine.  Decreased concentrations of refazodone.  Phenytoin, see Anticonvulsants (Hydantoins)  Primidone Decreased concentrations of carbamazepine, primidone, and phenobarbital (metabolite of primidone).  Propoxyphene Increased concentrations of carbamazepine.  Propoxyphene Increased concentrations of carbamazepine.  Increased concentrations of carbamazepine.  Propoxyphene Increased concentrations of carbamazepine.  Increased concentrations of carbamazepine, primidone, and phenobarbital (metabolite of primidone).  Avoid combination of carbamazepine.  Avoid combination of carbamazepine, primidone, and phenobarbital (metabolite of primidone).  Avoid combination of carbamazepine.  Decreased concentrations of carbamazepine.  Avoid combination of carbamazepine.  Decreased concentrations of carbamazepine.	Diltiazem		Monitor carbamazepine concentrations. Decrease carbamazepine dose if necessary.
Fluoxetine Increased concentrations of carbamazepine.  Grapefruit Juice Increased concentrations of carbamazepine do if necessary.  Haloperidol, see Sedatives/Hypnotics/Agents used in Psychiatry (Antipsychotic Agents Isoniazid Increased risk of carbamazepine toxicity and isoniazid hepatotoxicity.  Lamotrigine, see Anticonvulsants  Lithium, see Sedative/Hypnotics/Agents used in Psychiatry, Antidepressants (Miscellaneous Antidepressants)  Macrolide Antibiotics Increased concentrations of carbamazepine.  MAO Inhibitors (Isocarboxazid, phenelzine, tranylcypromine) Increased risk of severe adverse effects (hyperpyrexia, hyperexcitability, muscle rigidity, seizures).  Nefazodone Increased concentrations of carbamazepine.  Decreased concentrations of carbamazepine.  Decreased concentrations of carbamazepine.  Phenytoin, see Anticonvulsants (Hydantoins)  Primidone Decreased concentrations of carbamazepine, primidone, and phenobarbital (metabolite of primidone).  Increased concentrations of carbamazepine.  Decreased concentrations of carbamazepine, primidone, and phenobarbital (metabolite of primidone).  Propoxyphene Increased concentrations of carbamazepine.  Propoxyphene Increased concentrations of carbamazepine.  Increased concentrations of carbamazepine.  Propoxyphene Increased concentrations of carbamazepine.  Propoxyphene Increased concentrations of carbamazepine.  Propoxyphene Increased concentrations of carbamazepine.	Doxycycline, see Antimicrobia	al Agents, Antibacterial Antibiotics (1	Tetracyclines)
Grapefruit Juice Increased concentrations of carbamazepine.  Haloperidol, see Sedatives/Hypnotics/Agents used in Psychiatry (Antipsychotic Agents Isoniazid Increased risk of carbamazepine toxicity and isoniazid hepatotoxicity.  Lamotrigine, see Anticonvulsants  Lithium, see Sedative/Hypnotics/Agents used in Psychiatry, Antidepressants  Macrolide Antibiotics Increased in Psychiatry, Antidepressants  Macrolide Antibiotics Increased concentrations of carbamazepine.  Increased concentrations of carbamazepine.  MAO Inhibitors [isocarboxazid, phenelzine, tranylcypromine] Increased concentrations of carbamazepine.  Decreased concentrations of carbamazepine.  Phenytoin, see Anticonvulsants (Hydantoins)  Primidone Decreased concentrations of carbamazepine, primidone, and phenobarbital (metabolite of primidone).  Propoxyphene Increased concentrations of carbamazepine.  Decreased concentrations of carbamazepine.  Decreased concentrations of carbamazepine.  Decreased concentrations of carbamazepine.  Propoxyphene Increased concentrations of carbamazepine.  Decreased concentrations of carbamazepine.  Decreased concentrations of carbamazepine.  Avoid combination if possible. Otherw monitor carbamaz primidone concentrations of carbamazepine.  Propoxyphene Increased concentrations of carbamazepine.	Felodipine, see Antihypertens	sive and Cardiovascular Agents (Calc	ium-Channel Blockers)
Isoniazid Increased risk of carbamazepine toxicity and isoniazid hepatotoxicity.  Lamotrigine, see Anticonvulsants  Lithium, see Sedative/Hypnotics/Agents used in Psychiatry, Antidepressants  Macrolide Antibiotics (Clarithromycin, erythromycin, troleandomycin)  MAO Inhibitors (isocarboxazid, phenelzine, tranylcypromine)  Nefazodone Increased concentrations of carbamazepine.  Decreased concentrations of carbamazepine, primidone, and phenobarbital (metabolite of primidone).  Propoxyphene Increased concentrations of carbamazepine.  Discontinue MAO Avoid combination of carbamazepine, primidone, and phenobarbital (metabolite of primidone).  Propoxyphene Increased concentrations of carbamazepine.  Decreased concentrations of carbamazepine.  Nonitor carbamazepine doi functional prossible. Otherw monitor carbamazente concentrations of carbamazepine.	Fluoxetine		Monitor carbamazepine concentrations. Decrease carbamazepine dose if necessary.
Increased risk of carbamazepine toxicity and isoniazid hepatotoxicity.	Grapefruit Juice		Avoid combination.
Carbamazepine toxicity and isoniazid hepatotoxicity.   Monitor carbamaze concentrations. Decarbamazepine do if necessary.	Haloperidol, see Sedatives/Hy	ypnotics/Agents used in Psychiatry (	Antipsychotic Agents)
Lithium, see Sedative/Hypnotics/Agents used in Psychiatry, Antidepressants  Macrolide Antibiotics [clairthromycin, of carbamazepine. on concentrations and decrease dose if not adverse effects (hyperpyrexia, hyperexcitability, muscle rigidity, seizures). of carbamazepine. On carbamazepine. On carbamazepine. On carbamazepine. On carbamazepine. On carbamazepine, primidone of carbamazepine, and phenobarbital (metabolite of primidone). On carbamazepine.	Isoniazid	carbamazepine toxicity	Monitor liver function tests Monitor carbamazepine concentrations. Decrease carbamazepine dose if necessary.
Macrolide Antibiotics   Increased concentrations of carbamazepine.   Avoid combination if possible. Otherw monitor carbamaze concentrations and decrease dose if n	Lamotrigine, see Anticonvulsa	ants	
[clarithromycin, erythromycin, troleandomycin]  MAO Inhibitors [isocarboxazid, phenelzine, tranylcypromine]  Nefazodone Increased risk of severe adverse effects (hyperpyrexia, hyperexcitability, muscle rigidity, seizures).  Nefazodone Increased concentrations of carbamazepine. Decreased concentrations of nefazodone.  Phenytoin, see Anticonvulsants (Hydantoins)  Primidone Decreased concentrations of carbamazepine, primidone, and phenobarbital (metabolite of primidone).  Propoxyphene Increased concentrations of carbamazepine.  Propoxyphene Increased concentrations of carbamazepine.  Increased concentrations of carbamazepine.  Monitor carbamaz primidone concent adjust dose of one drugs as needed.  Avoid combination in primidone concentrations of carbamazepine.  Monitor carbamaz primidone concentrations of carbamazepine.  Monitor carbamaz primidone concentrations of carbamazepine.  Monitor carbamaz primidone concentrations of carbamazepine.			pressants
[isocarboxazid, phenelzine, tranylcypromine] adverse effects (hyperpyrexia, hyperexcitability, muscle rigidity, seizures).  Nefazodone Increased concentrations of carbamazepine. Decreased concentrations of nefazodone.  Phenytoin, see Anticonvulsants (Hydantoins)  Primidone Decreased concentrations of carbamazepine, primidone, and phenobarbital (metabolite of primidone).  Propoxyphene Increased concentrations of carbamazepine.  Nonitor carbamaz primidone concent Adjust dose of one drugs as needed.  Avoid combination of carbamazepine.  Monitor carbamaz primidone concent Adjust dose of one drugs as needed.  Avoid combination of carbamazepine.	[clarithromycin, erythromycin,		Avoid combination if possible. Otherwise, monitor carbamazepine concentrations and decrease dose if necessar
of carbamazepine. Decreased concentrations of nefazodone.  Phenytoin, see Anticonvulsants (Hydantoins)  Primidone  Decreased concentrations of carbamazepine, primidone, and phenobarbital (metabolite of primidone).  Propoxyphene  Increased concentrations of carbamazepine.  Avoid combination if possible. Otherw monitor carbamaze concentrations and carbamaze concentrations and carbamaze concentrations and carbamaze concentrations and concentrations and carbamaze concentrations carbamaze car	[isocarboxazid, phenelzine,	adverse effects (hyperpyrexia, hyperexcitability, muscle rigidity,	Avoid combination. Discontinue MAO inhibitor at least 14 days prior to starting carbamazepine.
Primidone  Decreased concentrations of carbamazepine, primidone, and phenobarbital (metabolite of primidone).  Propoxyphene  Increased concentrations of carbamazepine.  Monitor carbamaz primidone concent Adjust dose of one drugs as needed.  Avoid combination if possible. Otherw monitor carbamaze concentrations an	Nefazodone	of carbamazepine. Decreased concentrations	Avoid combination.
of carbamazepine, primidone, and phenobarbital Adjust dose of one drugs as needed.  Propoxyphene Increased concentrations of carbamazepine. Avoid combination if possible. Otherw monitor carbamaze concentrations an	Phenytoin, see Anticonvulsan	ts (Hydantoins)	
of carbamazepine. if possible. Otherv monitor carbamaze concentrations an	Primidone	of carbamazepine, primidone, and phenobarbital	Monitor carbamazepine at primidone concentrations. Adjust dose of one or both drugs as needed.
400,040,400,111	Propoxyphene		Avoid combination if possible. Otherwise, monitor carbamazepine concentrations and decrease dose if necessal
[amitriptyline, desipramine, doxepin, imipramine, Decreased concentrations tricyclic antidepreconcentrations. A	[amitriptyline, desipramine, doxepin, imipramine,	of carbamazepine. Decreased concentrations	Monitor carbamazepine an tricyclic antidepressant concentrations. Adjust do of one or both drugs as needed.

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT		
	Valproic acid, see Anticonvulsants				
	Verapamil	Increased concentrations of carbamazepine.	Monitor carbamazepine concentrations. Decrease carbamazepine dose if necessary.		
	Warfarin, see Anticoagulants	/Thrombolytic Agents			
Lamotrigine	Carbamazepine	Decreased concentrations of lamotrigine. Increased risk of carbamazepine toxicity.	Adjust dose of lamotrigine as needed when starting, stopping, or changing dose of carbamazepine.		
	Valproic Acid [divalproex sodium, valproic acid, valproate sodium]	Increased concentrations of lamotrigine. Decreased concentrations of valproic acid.	Adjust dose of one or both drugs as needed.		
Phenobarbital	Beta-Blockers [metoprolol, propranolol]	Decreased bioavailability of beta-blocker.	Increase beta-blocker dose if necessary.		
	Corticosteroids, see Corticos	teroids—Barbiturates			
	Doxycycline, see Antimicrobi (Tetracyclines)—Barbiturate	al Agents, Antibacterial Antibiotics s			
	Estrogens, see Miscellaneou	s Agents—Barbiturates			
	Ethanol, see Miscellaneous Agents—Barbiturates				
	Felodipine, see Antihypertensive and Cardiovascular Agents (Calcium-Channel Blockers)—Barbiturates				
	Griseofulvin, see Antimicrobial Agents (Miscellaneous Antifungals)—Barbiturates				
	Methadone, see Pain Medications (Narcotic)—Barbiturates				
	Metronidazole, see Antimicrobial Agents (Miscellaneous Antibacterial Antibiotics)—Barbiturates				
	Nifedipine, see Antihypertens (Calcium-Channel Blockers)	sive and Cardiovascular Agents —Barbiturates			
	Quinidine, see Antihypertensive and Cardiovascular Agents (Antiarrhythmic Agents)—Barbiturates				
	Theophylline, see <i>Bronchodil</i>	lators—Barbiturates			
	Valproic Acid	Increased concentrations of phenobarbital.	Decrease phenobarbital dose if necessary.		
	Voriconazole, see Antimicrobial Agents (Azole Antifungals)—Barbiturates				
	Warfarin, see Anticoagulants/Thrombolytic Agents—Barbiturates				
Hydantoins [ethotoin, fosphenytoin, mephenytoin, phenytoin]	Amiodarone	Increased concentrations of phenytoin. Decreased concentrations of amiodarone.	Monitor phenytoin concentrations* and signs/symptoms of phenytoin toxicity. Monitor		
*Monitor free (unbound) phenytoin concentrations in patients with renal insufficiency or failure.		or announce.	for loss of amiodarone effect. Adjust doses of one or both drugs as needed.		
	Anticoagulants [anisidione, dicumarol, warfarin]	Increased concentrations of phenytoin. Increased INR and risk of bleeding.	Monitor for altered response to phenytoin or anticoagulan Monitor phenytoin concentrations* and INR. Adjust dose of one or both drugs as needed.		

INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
Antineoplastic Agents [bleomycin, carboplatin, carmustine, cisplatin, methotrexate, vinblastine]	Decreased concentrations of phenytoin.	Monitor phenytoin concentrations.* Increase phenytoin dose if necessary
Carbamazepine	Decreased concentrations of carbamazepine. Variable effects on concentrations of phenytoin.	Monitor carbamazepine and phenytoin concentrations*. Adjust dose of one or both drugs as needed.
Chloramphenicol	Increased concentrations of phenytoin. Variable effects on concentrations of chloramphenicol.	Monitor phenytoin concentrations.* Adjust dose of one or both drugs as needed.
Cimetidine	Increased concentrations of phenytoin.	Avoid combination. Use alternative histamine H <sub>2</sub> -antagonist (eg, ranitidine
Corticosteroids, see Corticos	teroids—Hydantoins	
Cyclosporine, see <i>Transplant</i>	Immunosuppressants—Hydantoins	
Diazoxide	Decreased concentrations of phenytoin.	Monitor phenytoin concentrations.* Increase phenytoin dose if necessary.
Disopyramide, see Antihyper (Antiarrhythmic Agents)—Hy	tensive and Cardiovascular Agents Idantoins	
Disulfiram	Increased concentrations of phenytoin.	Monitor phenytoin concentrations.* Decrease phenytoin dose if necessary.
Dopamine	Increased risk of profound hypotension and cardiac arrest.	Monitor blood pressure. Discontinue phenytoin if hypotension occurs.
Doxycycline, see Antimicrobi (Tetracyclines)—Hydantoins	al Agents, Antibacterial Antibiotics	
Estrogens, see Miscellaneou	s Agents—Hydantoins	
Felbamate	Increased concentrations of phenytoin. Decreased concentrations of felbamate.	Monitor felbamate and phenytoin concentrations.* Adjust dose of one or both drugs as needed.
Felodipine, see Antihypertens (Calcium-Channel Blockers)-	sive and Cardiovascular Agents —Hydantoins	
Fluconazole	Increased concentrations of phenytoin.	Monitor phenytoin concentrations.* Decrease phenytoin dose if necessary.
Fluoxetine	Increased concentrations of phenytoin.	Monitor phenytoin concentrations.* Decrease phenytoin dose if necessary.
Folic acid	Decreased concentrations of phenytoin.	Monitor phenytoin concentrations.* Increase phenytoin dose if necessary.
Isoniazid	Increased concentrations of phenytoin.	Monitor phenytoin concentrations.* Decrease phenytoin dose if necessary.
Itraconazole, see Antimicrob	ial Agents ( Azole Antifungals)—Hyda	antoins

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT		
	Methadone, see Pain Medicat	tions (Narcotic)—Hydantoins			
	Metyrapone, see Miscellaneo	us Agents—Hydantoins			
	Mexiletine, see Antihypertens (Antiarrhythmic Agents)—Hyd	ive and Cardiovascular Agents, lantoins			
	Nisoldipine, see Antihypertensive Agents and Cardiovascular Agents (Calcium-Channel Blockers)—Hydantoins				
	Phenacemide	Increased concentrations of phenytoin.	Monitor phenytoin concentrations.* Decrease phenytoin dose if necessary.		
	Phenylbutazones [oxyphenbutazone, phenylbutazone]	Increased concentrations of phenytoin.	Monitor phenytoin concentrations.* Decrease phenytoin dose if necessary.		
	Primidone	Increased concentrations of primidone and primidone-metabolite.	Monitor primidone and primidone-metabolite concentrations. Decrease primidone dose if necessary.		
	Quinidine, see Antihypertensiv	ve and Cardiovascular Agents (Anti	iarrhythmic Agents)—Hydantoins		
	Rifamycins [rifabutin, rifampin]	Decreased concentrations of phenytoin.	Monitor phenytoin concentrations.* Increase phenytoin dose if necessary.		
	Sertraline	Increased concentrations of phenytoin.	Monitor phenytoin concentrations.* Decrease phenytoin dose if necessary.		
	Sucralfate	Decreased GI absorption of phenytoin.	Monitor phenytoin concentrations.* Increase phenytoin dose if necessary.		
	Sulfonamides [sulfadiazine, sulfamethizole]	Increased concentrations of phenytoin.	Monitor phenytoin concentrations.* Decrease phenytoin dose if necessary.		
	Tacrolimus, see Transplant Imi	munosuppressants			
	Theophylline, see Bronchodila	tors			
	Ticlopidine	Increased concentrations of phenytoin.	Monitor phenytoin concentrations.* Decrease phenytoin dose if necessary.		
	Trimethoprim	Increased concentrations of phenytoin.	Monitor phenytoin concentrations.* Decrease phenytoin dose if necessary.		
	Valproic Acid [divalproex sodium, valproic acid]	Increased concentrations of phenytoin. Decreased concentrations of valproic acid.	Monitor free phenytoin and valproic acid concentrations. Adjust dose of one or both both drugs as needed.		
Valproic Acid [divalproex sodium, sodium valproate, valproic acid]	Barbiturates [phenobarbital, primidone]	Increased concentrations of barbiturate.	Increase barbiturate dose if necessary.		
	Carbamazepine	Decreased concentrations of valproic acid.	Monitor valproic acid concentrations, seizure activity, and signs/symptoms of toxicity for at least a month after starting or stopping either drug. Increase valproic acid dose if necessary.		

INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
Cholestyramine	Decreased GI absorption of valproic acid.	Separate administration times by at least 3 hours. Monitor valproic acid concentrations. Increase valproic acid dose if necessary.
Felbamate	Increased concentrations of valproic acid.	Monitor valproic acid concentrations. Decrease valproic acid dose if necessary.
Lamotrigine, see Anticonvu	Isants	
Phenytoin, see <i>Anticonvuls</i>	ants	
Salicylates [aspirin, bismuth subsalicylate, choline salicylate, magnesium salicylate, salsalate, sodium salicylate sodium thiosalicylate]	Increased free (unbound) concentrations of valproic acid.	Monitor free valproic acid concentrations. Decrease valproic acid dose if necessary.

Azathioprine		Allopurinol, see Arthritis and Gout Agents (Miscellaneous Arthritis and Gout Agents)—Thiopurines		
Methotrexate	NSAIDs (diclofenac, etodolac, fenoprofen, flubiprofen, ibuprofen, indomethacin, ketoprofen, ketorolac, meclofenamate, mefenamic acid, nabumetone, naproxen, oxaprozin, piroxicam, sulindac, tolmetin]	Increased risk of methotrexate toxicity.	Monitor for renal impairment and signs/symptoms of toxicity. Monitor methotrexate concentrations. Consider extended leucovorin rescue therapy.	
	Penicillins [amoxicillin, ampicillin, bacampicillin, carbenicillin, cloxacillin, dicloxacillin, methicillin, mezlocillin, penicillin G, penicillin V, piperacillin, ticarcillin]	Increased concentrations of methotrexate. Increased risk of methotrexate toxicity.	Monitor for signs/symptoms of toxicity. Monitor methotrexate concentrations. Consider extended leucovorin rescue therapy. Use alternative anbiotic if possible (eg, ceftazidime).	
	Probenecid	Increased concentrations of methotrexate. Increased risk of methotrexate toxicity.	Decrease methotrexate dose. Monitor for signs/symptoms of toxicity. Monitor methotrexate concentrations. Consider extended leucovorin rescue therapy.	
	Salicylates [aspirin, bismuth subsalicylate, choline magnesium salicylate, choline salicylate, magnesium salicylate, salsalate, sodium salicylate, sodium thiosalicylate]	Increased risk of methotrexate toxicity.	Decrease methotrexate dose. Monitor for signs/symptoms of toxicity. Monitor methotrexate concentrations. Consider extended leucovorin rescue therapy.	

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
	Sulfonamides [sulfadiazine, sulfamethizole, sulfamethoxazole, sulfasalazine, sulfisoxazole, trimethoprim/ sulfamethoxazole]	Increased risk of bone marrow suppression and megaloblastic anemia.	Avoid combination if possible. Otherwise, monitor for signs/symptoms of hematologic toxicity. Administer leucovorin if necessary.
<u>ANTIPARKINSON</u>			
Levodopa	Hydantoins [ethotoin, fosphenytoin, mephenytoin, phenytoin]	Decreased effects of levodopa.	Avoid combination.
	Iron Salts (Oral) [ferrous fumarate, ferrous gluconate, ferrous sulfate, iron polysaccharide]	Decreased effects of levodopa.	Separate administration times. Monitor clincial response and increase levodopa dose if necessary.
	MAO Inhibitors [phenelzine, tranylcypromine]	Increased risk of hypertensive reactions.	Avoid combination. Use alternative MAOI (eg, selegiline).
	Pyridoxine	Decreased effects of levodopa.	Avoid combination if possible in patients treated with levodopa alone.
ARTHRITIS AND (	GOUT AGENTS		
Allopurinol	Ampicillin, see Antimicrobial A	Agents (Penicillins)	
	Thiopurines [azathioprine, mercaptopurine]	Increased effects of thiopurine.	Decrease thiopurine dose by 25-33%. Monitor hematologic function (bone marrow suppression).
Colchicine	Cyclosporine, see Transplant Immunosuppressants		
Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)	Diclofenac, Diflunisal, Etodolac, Fenoprofen, Flubiprofen, Ibuprofen, Indomethacin, Ketoprofen, Ketorolac, Meclofenamate, Mefenamic Acid, Nabumetone, Naproxen, Piroxicam, Sulindac, Tolmetin		
Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)-class	Aminoglycosides, see Antimic	robial Agents (Antibacterial Antibio	tics)
	Beta-Blockers, see Antihypert (Cardio-Selective and Noncar	tensive and Cardiovascular Agents dio-Selective Beta-Blockers)	
	Lithium, see Sedatives/Hypnot (Miscellaneous Antidepressar	tics/Agents used in Psychiatry, Antic nts)	depressants
	Methotrexate, see Antineopla		
	Warfarin, see Anticoagulants/		
<b>Diflunisal</b> (see also Nonsteroidal Anti-Inflammatory Drugs-class)	Probenecid	Increased effects of diflunisal.	Monitor for diflunisal toxicity.
Ibuprofen (see also Nonsteroidal Anti-Inflammatory Drugs-class)	Beta-Blockers, see Antihypertensive and Cardiovascular Agents (Cardio-Selective and Noncardio-Selective Beta-Blockers) — NSAIDs		
Indomethacin (see also Nonsteroidal Anti-Inflammatory Drugs-class)		tensive and Cardiovascular Agents dio-Selective Beta-Blockers) — NS.	AIDs

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT	
		e and Cardiovascular Agents sive and Cardiovascular Agents)		
Ketorolac (see also Nonsteroidal Anti-Inflammatory Drugs-class)	Probenecid	Increased risk of ketorolac toxicity.	Avoid combination.	
	Salicylates [aspirin]	Increased risk of ketorolac adverse effects.	Avoid combination.	
<b>Naproxen</b> (see also Nonsteroidal Anti-Inflammatory Drugs-class)		rtensive and Cardiovascular Agen ardio-Selective Beta-Blockers) — .		
<b>Piroxicam</b> (see also Nonsteroidal Anti-Inflammatory Drugs-class)		Beta-Blockers, see Antihypertensive and Cardiovascular Agents (Cardio-Selective and Noncardio-Selective Beta-Blockers) — NS.		
	Ritonavir	Increased risk of piroxicam toxicity.	Avoid combination.	
<b>BRONCHODILAT</b>	ORS			
Theophyllines	Aminophylline, Dyphyl	Aminophylline, Dyphylline, Oxtriphylline, Theophylline		
Theophyllines-class	Acyclovir	Increased concentrations of theophylline.	Monitor theophylline concentrations. Decrease	

		piroxicam toxicity.	
<b>BRONCHODILAT</b>	ORS		
Theophyllines	Aminophylline, Dyphylli	ine, Oxtriphylline, Theophyl	line
Theophyllines-class	Acyclovir	Increased concentrations of theophylline.	Monitor theophylline concentrations. Decrease theophylline dose if necessary.
	Barbiturates [amobarbital, aprobarbital, butabarbital, butalbital, mephobarbital, pentobarbital, phenobarbital, primidone, secobarbital]	Decreased concentrations of theophylline.	Monitor theophylline concentrations. Increase theophylline dose if necessary.
	Beta-Blockers, noncardio-selective [carteolol, penbutolol, pindolol, propranolol, timolol]	Increased concentrations of theophylline. Pharmacologic antagonism may decrease effects of one or both drugs.	Monitor theophylline concentrations. Use cardioselective beta-blockers.
	Cimetidine	Increased concentrations of theophylline.	Monitor theophylline concentrations. Decrease theophylline dose by 20-40% when starting cimetidine. Use alternative histamine H <sub>2</sub> -antagonist (eg, ranitidine).
	Contraceptives, Oral	Increased concentrations of theophylline.	Monitor theophylline concentrations. Decrease theophylline dose if necessary.
	Diltiazem	Increased concentrations of theophylline.	Monitor theophylline concentrations. Decrease theophylline dose if necessary.
	Disulfiram	Increased concentrations of theophylline.	Monitor theophylline concentrations. Decrease theophylline dose if necessary.
	Food	Increased or decreased absorption or clearance of various theophylline products.	Refer to package insert for specific management.

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
	Halothane	Increased risk of arrhythmias.	Avoid combination. Use alternative anesthetic (eg, enflurane).
	Hydantoins [fosphenytoin, phenytoin]	Decreased concentrations of theophylline and phenytoin.	Monitor theophylline and phenytoin concentrations. Adjust dose of one or both drugs as needed.
	Macrolide Antibiotics [azithromycin, clarithromycin, dirithromycin, erythromycin, troleandomycin]	Increased concentrations of theophylline.	Monitor theophylline concentrations. Decrease theophylline dose if necessary. Use alternative antibiotic.
	Mexiletine	Increased concentrations of theophylline.	Monitor theophylline concentrations. Decrease theophylline dose if necessary.
	Quinolones [ciprofloxacin, enoxacin, norfloxacin]	Increased concentrations of theophylline.	Monitor theophylline concentrations. Decrease theophylline dose if necessary.
	Rifamycins [rifabutin, rifampin, rifapentine]	Decreased concentrations of theophylline.	Monitor theophylline concentrations. Increase theophylline dose if necessary.
	Thiabendazole	Increased concentrations of theophylline.	Monitor theophylline concentrations. Decrease theophylline dose if necessary.
	Thioamines [methimazole, propylthiouracil]	Decreased theophylline concentrations in hyperthyroid patients; returns to normal once euthyroid state achieved.	Monitor theophylline concentrations. Adjust theophylline dose as needed. Achieve euthyroid state as soon as possible.
	Thyroid Hormones [dextrothyroxine, levothyroxine, liothyronine, liotrix, thyroglobulin, thyroid]	Decreased theophylline concentrations in hyperthyroid patients; returns to normal once euthyroid state achieved.	Monitor theophylline concentrations. Adjust theophylline dose as needed. Achieve euthyroid state as soon as possible.
	Ticlopidine	Increased concentrations of theophylline.	Monitor theophylline concentrations. Decrease theophylline dose if necessary.
	Zileuton	Increased concentrations of theophylline.	Monitor theophylline concentrations. Decrease theophylline dose by 50% when starting zileuton.
Leukotriene Inhibitors			
Zileuton	Theophylline, see <i>Bronchodila</i>	tors	

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT		
CORTICOSTEROI	DS				
Corticosteroids		otropin, Cortisone, Cosyntro cortisone, Methylprednisol one			
Corticosteroids-class	Anticholinesterases [ambenonium, edrophonium, neostigmine, pyridostigmine]	Corticosteroids antagonize effect of anticholinesterases in myasthenia gravis.	Monitor clinical response.		
	Aspirin, see Pain Medications (Non-Narcotic)				
	Barbiturates [amobarbital, aprobarbital, butabarbital, butalbital, mephobarbital, pentobarbital, phenobarbital, primidone, secobarbital]	Decreased effects of corticosteroid.	Avoid combination if possible. Otherwise, increase corticosteroid dose if necessary.		
	Hydantoins [ethotoin, fosphenytoin, mephenytoin, phenytoin]	Decreased effects of corticosteroid.	Increase corticosteroid dose if necessary.		
	Rifamycins [rifabutin, rifampin, rifapentine]	Decreased effects of corticosteroid.	Avoid combination if possible Otherwise, increase corticosteroid dose if necessary.		
<b>Dexamethasone</b> (see also Corticosteroids-class)	Aminoglutethimide	Decreased effects of dexamethasone.	Increase dexamethasone dose if necessary. Use alternative corticosteroid (eg, hyrdrocortisone).		
	Azole Antifungals [fluconazole, itraconazole, ketoconazole]	Increased effects of dexamethasone.	Decrease dexamethasone dose if necessary.		
Hydrocortisone (see also Corticosteroids-class)	Azole Antifungals [fluconazole, itraconazole, ketoconazole]	Increased effects of hydrocortisone.	Decrease hydrocortisone dose if necessary.		
	Bile Acid Sequestrants [cholestyramine, colestipol]	Decreased GI absorption of hydrocortisone.	Separate administration times. Use alternative lipid-lowering drug.		
	Estrogens (chlorotrianisene, conjugated estrogens, diethylstilbesterol, esterified estrogens, estradiol, estrone, estropipate, ethinyl estradiol, quinestrol]	Increased effects of hydrocortisone.	Decrease hydrocortisone dose if necessary.		
Methylprednisolone (see also Corticosteroids-class)	Azole Antifungals [fluconazole, itraconazole, ketoconazole]	Increased effects of methylprednisolone.	Decrease methylprednisolone dose if necessary.		
	Macrolide Antibiotics [erythromycin, troleandomycin]	Increased effects of methylprednisolone.	Decrease methylprednisolone dose if necessary.		
Prednisolone and Prednisone (see also Corticosteroids-class)	Azole Antifungals [fluconazole, itraconazole, ketoconazole]	Increased effects of corticosteroid.	Decrease corticosteroid dose if necessary.		

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DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT	
	Estrogens [chlorotrianisene, conjugated estrogens, diethylstilbesterol, esterified estrogens, estradiol, estrone, estropipate, ethinyl estradiol, quinestrol]	Increased effects of corticosteroid.	Decrease corticosteroid dose if necessary.	
DIURETICS				
Loop Diuretics	Bumetanide, Ethacrynic Acid, Furosemide, Torsemide			
Loop Diuretics-class	Aminoglycosides, see Antimic	robial Agents (Antibacterial Antibio	tics)	
	Cisplatin	Increased risk of ototoxicity.	Avoid combination if possible Otherwise, monitor hearing function.	
	Digoxin, see Antihypertensive (Miscellaneous Antihypertens	and Cardiovascular Agents ive and Cardiovascular Agents)		
	Thiazide Diuretics [bendroflumethiazide, benzthiazide, chlorothiazide, chlorthalidone, hydrochlorothiazide, hydroflumethiazide, indapamide, methyclothiazide, metolazone, polythiazide, quinethazone, trichlormethiazide]	Profound diuresis and electrolyte disturbances.	Adjust diuretic dose as needed. Monitor electrolyte abnormalities and hydration status when starting combination therapy.	
Furosemide (see also Loop Diuretics-class)	Cholestyramine	Decreased GI absorption of furosemide.	Administer cholestyramine at least 2 hours after furosemide.	
	Colestipol	Decreased GI absorption of furosemide.	Administer colestipol at least 2 hours after furosemide.	
Thiazide Diuretics	Bendroflumethiazide, Benzthiazide, Chlorothiazide, Chlorthalidone, Hydrochlorothiazide, Hydroflumethiazide, Indapamide, Methyclothiazide, Metolazone, Polythiazide, Quinethazone, Trichlormethiazide			
Thiazide Diuretics-class	Digoxin, see Antihypertensive (Miscellaneous Antihypertens	and Cardiovascular Agents ive and Cardiovascular Agents)		
	Lithium, see Sedative/Hypnotics/Agents used in Psychiatry, Antidepressants (Miscellaneous Antidepressants)			
	Loop Diuretics, see <i>Diuretics</i>			
	Sulfonylureas, see Hypoglycei	mic Agents		
<b>GASTROINTESTIN</b>	IAL AGENTS			
Histamine H <sub>2</sub> -Antagonists	Cimetidine, Famotidine,	Nizatidine, Ranitidine		
Histamine H <sub>2</sub> -Antagonists-class	Ketoconazole, see Antimicrob	ial Agents (Azole Antifungals)		
Cimetidine (see also Histamine H <sub>2</sub> -Antagonists-class)	Beta-Blockers, see Antihypert (Cardio-Selective and Noncar	ensive and Cardiovascular Agents dio-Selective Beta-Blockers)		
	Carbamazepine, see Anticonv	ulsants		
	Lidocaine, see Antihypertensi	ve and Cardiovascular Agents (Antia	arrhythmic Agents)	

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT	
	Metformin, see <i>Hypoglycemia</i>	: Agents		
	Moricizine, see Antihypertensive and Cardiovascular Agents (Antiarrhythmic Agents)			
	Nifedipine, see Antihypertens	ive and Cardiovascular Agents (Cald	cium-Channel Blockers)	
	Phenytoin, see Anticonvulsan	ts—Hydantoins		
	Praziquantel	Increased concentrations of praziquantel.	Monitor for toxicity. Use alternative histamine H <sub>2</sub> -antagonist (eg, ranitidine).	
	Procainamide, see Antihypert	tensive and Cardiovascular Agents (.	Antiarrhythmic Agents)	
	Quinidine, see Antihypertensi	arrhythmic Agents)		
	Theophylline, see <i>Bronchodila</i>			
	Tricyclic Antidepressants, see	e Sedatives/Hypnotics/Agents used	in Psychiatry (Antidepressants)	
	Warfarin, see Anticoagulants,	/Thrombolytic Agents		
Phosphate Binders/Antacids	(Calcium Carbonate, Ca	num Carbonate, Aluminum H Alcium Acetate), Magnesium e, Magnesium Hydroxide)		
Phosphate Binders/ Antacids-class	Iron Salts, Oral, see Anemia A	Agents (Iron Products)		
	Ketoconazole, see Antimicrob	nial Agents (Azole Antifungals)		
	Quinidine, see Antihypertensive and Cardiovascular Agents (Antiarrhythmic Agents)			
	Quinolones, see Antimicrobial Agents (Antibacterial Antibiotics)			
	Sodium Polystyrene Sulfonate (Kayexalate), see Gastrointestinal Agents (Miscellaneous Gastrointestinal Agents)			
	Tetracyclines, see Antimicrob	ial Agents (Antibacterial Antibiotics	)	
Calcium Carbonate (see also Phosphate Binders/Antacids-class)	Verapamil, see Antihypertens (Calcium-Channel Blockers)—	ive and Cardiovascular Agents -Calcium Salts		
Calcium Acetate (see also Phosphate Binders/Antacids-class)	Verapamil, see Antihypertens (Calcium-Channel Blockers)—	ive and Cardiovascular Agents -Calcium Salts		
Sevelamer		lies were performed in humans. The omitantly administered drugs and de		
Proton Pump Inhibitors (PPIs)	Esomeprazole, Lansopr	azole, Omeprazole, Pantopra	azole, Rabeprazole	
Proton Pump Inhibitors-class	Itraconazole, see Antimicrobi	al Agents (Azole Antifungals)		
	Ketoconazole, see Antimicrob	nial Agents (Azole Antifungals)		
Miscellaneous Gastro	ointestinal Agents			
Metoclopramide	Cyclosporine, see <i>Transplant</i>	Immunosuppressants		
	Digoxin, see Antihypertensive (Miscellaneous Antihypertens	and Cardiovascular Agents sive and Cardiovascular Agents)		
Sodium Polystyrene Sulfonate (Kayexalate)	Phosphate Binders/Antacids [aluminum-magnesium hydroxide, calcium carbonate]	Increased risk of metabolic alkalosis. Decreased potassium binding effects of resin.	Separate administration times.	
Sucralfate	Quinolones, see Antimicrobia	l Agents (Antibacterial Antibiotics)		

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
HYPOGLYCEMIC A	AGENTS		
Insulin	Beta-Blockers, Noncardio- Selective [carteolol, nadolol, penbutolol, pindolol, propranolol, timolol]	Prolonged hypoglycemia with masking of hypoglycemic signs/symptoms (tachycardia)	Use cardio-selective beta-blocker. Monitor for signs/symptoms of hypoglycemia not affected by beta-blockers.
	Ethanol	Increased hypoglycemic effects of insulin.	Ingest ethanol in moderation and with meals.
	MAO Inhibitors [isocarboxazid, phenelzine, tranylcypromine]	Increased hypoglycemic effects of insulin.	Monitor blood glucose concentration. Decrease insulin dose if necessary.
	Salicylates [aspirin, bismuth subsalicylate, choline salicylate, magnesium salicylate, salsalate, sodium salicylate, sodium thiosalicylate]	Increased hypoglycemic effects of insulin.	Monitor blood glucose concentration. Decrease insulin dose if necessary.
Metformin	Cimetidine	Increased concentrations of metformin.	Monitor blood glucose concentration. Decrease metformin dose if necessary.
	lodinated Contrast Materials, IV	Increased risk of lactic acidosis.	Avoid combination. Discontinue metformin for at least 48 hours prior to and subsequent to the use of IV iodinated contrast materials.
Sulfonylureas	Acetohexamide, Chlorp Tolazamide, Tolbutamid	ropamide, Glimepride, Glipiz e	zide, Glyburide,
Sulfonylureas-class	Chloramphenicol	Increased hypoglycemic effects of sulfonylurea.	Monitor blood glucose concentration. Decrease sulfonylurea dose if necessary.
	Diazoxide	Decreased hypoglycemic effects of sulfonylurea.	Monitor blood glucose concentration. Increase sulfonylurea dose if necessary.
	Ethanol, see Miscellaneous A	gents	
	MAO Inhibitors [isocarboxazid, phenelzine, tranylcypromine]	Increased hypoglycemic effects of sulfonylurea.	Monitor blood glucose concentration. Decrease sulfonylurea dose if necessary.
	Phenylbutazones [oxyphenbutazone, phenylbutazone]	Increased hypoglycemic effects of sulfonylurea.	Monitor blood glucose concentration. Decrease sulfonylurea dose if necessary. Use alternative NSAID.
	Rifamycins [rifabutin, rifampin, rifapentine]	Decreased concentrations of sulfonylurea.	Monitor blood glucose concentration. Increase sulfonylurea dose if necessary.
	Salicylates [aspirin, choline salicylate, magnesium salicylate, salsalate, sodium salicylate, sodium thiosalicylate]	Increased hypoglycemic effects of sulfonylurea.	Monitor blood glucose concentration. Decrease sulfonylurea dose if necessary.

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
	Sulfonamides [sulfacytine, sulfadiazine, sulfamethizole, sulfamethoxazole, sulfasalazine, sulfisoxazole, multiple sulfonamides]	Increased concentrations of sulfonylurea. [Exception: Glyburide]	Monitor blood glucose concentration. Decrease sulfonylurea dose if necessary. Use noninteracting sulfonylurea (eg, glyburide).
	Thiazide Diuretics [bendroflumethiazide, benzthiazide, chlorothiazide, chlorthalidone, hydrochlorothiazide, hydroflumethiazide, indapamide, methyclothiazide, metolazone, polythiazide, quinethazone, trichlormethiazide]	Increased concentrations of fasting blood glucose. Decreased hypoglycemic effects of sulfonylurea.	Monitor blood glucose concentration. Increase sulfonylurea dose if necessary.
<b>Chlorpropamide</b> (see also Sulfonylureas-class)	Dicumarol	Increased hypoglycemic effects of chlorpropamide.	Monitor blood glucose concentration. Decrease chlorpropamide dose if necessary.
	Urinary Alkalinizers [potassium citrate, sodium acetate, sodium bicarbonate, sodium citrate, sodium lactate, tromethamine]	Increased elimination of chlorpropamide.	Monitor blood glucose concentration. Increase chlorpropamide dose if necessary.
<b>Glimepride</b> (see also Sulfonylureas-class)	Fluconazole	Increased hypoglycemic effects of tolbutamide.	Monitor blood glucose concentration. Decrease tolbutamide dose if necessary.
<b>Tolbutamide</b> (see also Sulfonylureas-class)	Dicumarol	Increased hypoglycemic effects of tolbutamide.	Monitor blood glucose concentration. Decrease tolbutamide dose if necessary.
	Fluconazole	Increased hypoglycemic effects of tolbutamide.	Monitor blood glucose concentration. Decrease tolbutamide dose if necessary.
	Sulfinpyrazone	Increased hypoglycemic effects of tolbutamide.	Monitor blood glucose concentration. Decrease tolbutamide dose if necessary.
HYPOLIPIDEMIC A	AGENTS		
Cholestyramine	Digoxin, see Antihypertensive and Cardiovascular Agents (Miscellaneous Antihypertensive and Cardiovascular Agents)		
	HMG-CoA Reductase Inhibitors, see Hypolipidemic Agents (Bile Acid Sequestrants)		
	Hydrocortisone, see Corticosteroids— Bile Acid Sequestrants		
	Furosemide, see Diuretics (Loc	op Diuretics)—Bile Acid Sequestra	nts
	Levothyroxine, see Miscellane	eous Agents	
	Valproic Acid, see Anticonvuls	sants	
	Warfarin, see Anticoagulants/	Thrombolytic Agents	
Clofibrate	Warfarin, see Anticoagulants/	Thrombolytic Agents	
Colestipol		s, see Hypolipidemic Agents—Bile	Acid Sequestrants
	Hydrocortisone, see Corticost	eroids—Bile Acid Sequestrants	

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
	Loop Diuretics, see Diuretics-	-Bile Acid Sequestrants	
Gemfibrozil	HMG-CoA Reductase Inhibitors, see Hypolipidemic Agents		
Probucol	Cyclosporine, see Transplant Immunosuppressants		
HMG-CoA Reductase Inhibitors (Statins)	Atorvastatin, Fluvastati	n, Lovastatin, Pravastatin, R	osuvastatin, Simvastatir
HMG-CoA Reductase Inhibitors-class	Azole Antifungals [fluconazole, itraconazole, ketoconazole, miconazole, voriconazole]	Increased risk of rhabdomyolysis.	Avoid combination if possibl Otherwise, monitor for signs/symptoms of statin toxicity. Decrease statin dose if necessary. Pravastatin is least affected by the interaction.
	Bile Acid Sequestrants [cholestyramine, colestipol]	Decreased GI absorption of HMG-CoA reductase inhibitor.	Separate administration times by at least 4 hours.
	Cyclosporine	Increased risk of rhabdomyolysis.	Avoid combination if possibl Otherwise, monitor for signs/symptoms of statin toxicity. Decrease statin dose if necessary.
	Diltiazem	Increased risk of rhabdomyolysis. [Exceptions: fluvastatin, pravastatin]	Avoid combination if possibl Otherwise, monitor for signs/symptoms of statin toxicity. Use noninteracting statin (eg, fluvastatin, pravastatin).
	Gemfibrozil	Increased risk of severe myopathy and rhabdomyolysis.	Avoid combination.
	Grapefruit Juice	Increased risk of rhabdomyolysis. [Exceptions: fluvastatin, pravastatin]	Avoid combination. Use noninteracting statin (eg, fluvastatin, pravastatin)
	Macrolide Antibiotics [azithromycin, clarithromycin, erythromycin]	Increased risk of severe myopathy and rhabdomyolysis. [Exceptions: fluvastatin, pravastatin]	Avoid combination. Use alternative antibiotic or noninteracting statin (eg, fluvastatin, pravastatin)
	Nefazodone	Increased risk of rhabdomyolysis. [Exceptions: fluvastatin, pravastatin]	Avoid combination. Use noninteracting statin (eg, fluvastatin, pravastatin)
	Rifamycins [rifabutin, rifampin, rifapentine]	Decreased effects of statin. [Exception: pravastatin]	Monitor clinical response. Use noninteracting statin (eg, pravastatin).
	Verapamil	Increased risk of rhabdomyolysis. [Exceptions: fluvastatin, pravastatin]	Avoid combination. Use noninteracting statin (eg, fluvastatin, pravastatin)
Lovastatin (see also HMG-CoA Reductase Inhibitors-class)	Cyclosporine	Increased risk of rhabdomyolysis.	Avoid combination. Report unexplained muscle pain, tenderness, or weakness.
PAIN MEDICATIO	NS		
Non-Narcotic			
Acetaminophen	Ethanol	Increased risk of acetaminophen-induced hepatotoxicity.	Avoid combination. Advise chronic ethanol consumers to avoid excessive or prolonged use of acetaminophen.

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT			
	Hydantoins [ethotoin, fosphenytoin, mephenytoin, phenytoin]	Increased risk of acetaminophen-induced hepatotoxicity.	Avoid chronic and excessive use of acetaminophen with regular hydantoin therapy.			
	Sulfinpyrazone	Increased risk of acetaminophen-induced hepatotoxicity.	Avoid chronic and excessive use of acetaminophen with regular sulfinpyrazone therapy.			
	Warfarin, see Anticoagulants	/Thrombolytic Agents				
Aspirin	Carbonic Anhydrase Inhibitors [acetazolamide, dichlorphenamide, methazolamide]	Increased risk of carbonic anhydrase inhibitor toxicity (CNS depression, metabolic acidosis).	Avoid combination.			
	Corticosteroids [betamethasone, cortisone, desoxycorticosterone, dexamethasone, fludrocortisone, hydrocortisone, methylprednisolone, paramethasone, prednisolone, triamcinolone]	Decreased effects of salicylate.	Monitor aspirin concentrations. Increase salicylate dose if necessary.			
	Heparin, see Anticoagulants/Thrombolytic Agents— Salicylates					
	Insulin, see Hypoglycemic Agents—Salicylates					
	Ketorolac, see Arthritis and Gout Agents (NSAIDs)—Salicylates					
	Methotrexate, see Antineoplastic Agents—Salicylates					
	Probenecid	Decreased uricosuric action of one or both drugs.	Avoid combination. Use non-antiinflammatory doses of aspirin.			
	Sulfonylureas, see Hypoglyco	emic Agents—Salicylates				
	Valproic acid, see Anticonvu	lsants—Salicylates				
	Warfarin, see Anticoagulants	Warfarin, see Anticoagulants/Thrombolytic Agents—Salicylates				
Narcotic						
Alfentanil	Ethanol, see <i>Miscellaneous A</i>	Agante				
Codeine	Quinidine	Decreased effects of codeine.	Use alternative analgesic.			
Fentanyl		ensive and Cardiovascular Agents (A				
Meperidine	MAO Inhibitors		Avoid combination.			
meperiaine	[isocarboxazid, phenelzine, selegiline, tranylcypromine]	Agitation, seizures, diaphoresis and fever. May progress to coma, apnea, and death.	Avoid combination.			
	Phenothiazines [chlorpromazine]	Excessive sedation and hypotension.	Avoid combination.			
	Ritonavir	Decreased efficacy of meperidine and increased risk of neurologic toxicity.	Avoid combination.			

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT	
Methadone	Barbiturates [amobarbital, aprobarbital, butabarbital, butalbital, mephobarbital, pentobarbital, phenobarbital, primidone, secobarbital]	Decreased effects of methadone. Possible with-drawal symptoms in patients on chronic methadone therapy.	Increase methadone dose if necessary.	
	Fluvoxamine	Increased concentrations of methadone.	Monitor clinical response when starting and stopping fluvoxamine in patients on chronic methadone therapy.	
	Hydantoins [ethotoin, fosphenytoin, mephenytoin, phenytoin]	Decreased effects of methadone. Possible with- drawal symptoms in patients on chronic methadone therapy.	Increase methadone dose if necessary.	
	Protease Inhibitors [nelfinavir, ritonavir]	Decreased effects of methadone. Possible with- drawal symptoms in patients on chronic methadone therapy.	Increased methadone dose if necessary.	
	Rifampin	Decreased effects of methadone. Possible with- drawal symptoms in patients on chronic methadone therapy.	Increase methadone dose if necessary.	
Morphine	Rifamycins [rifabutin, rifampin, rifapentine]	Decreased analgesic effects of morphine.	Monitor analgesic response Use alternative analgesic.	
Propoxyphene	Carbamazepine, see Anticonvulsants			
	Ritonavir	Increased risk of propoxyphene toxicity (seizures, respiratory depression, apnea, cardiac arrhythmias, pulmonary edema).	Avoid combination.	
SEDATIVES/HYPN	IOTICS/AGENTS USE	D IN PSYCHIATRY		
ANTIDEPRESSANTS Monoamine Oxidase Inhibitors (MAO Inhibitors)	Isocarboxazid, Phenelzi	ine, Selegiline, Tranylcyproi	mine	
Monoamine Oxidase (MAO) Inhibitors-class	Buproprion, see Sedatives/Hyp (Miscellaneous Antidepressan	onotics/Agents used in Psychiatry, A	Antidepressants	
	Carbamazepine, see Anticonvulsants			
	Insulin, see Hypoglycemic Agents			
	Levodopa, see Antiparkinson Agents			
	Meperidine, see Pain Medications (Narcotic)—MAO Inhibitors			
	Serotonin Reuptake Inhibitors, see Sedatives/Hypnotics/Agents used in Psychiatry (Antidepressants)			
	Sibutramine, see Miscellaneous Agents			
	Sulfonylureas, see Hypoglycemic Agents			
	Tricyclic Antidepressants, see Sedatives/Hypnotics/Agents used in Psychiatry (Antidepressants,			
Serotonin Reuptake Inhibitors	Citolapram, Escitalopra Paroxetine, Sertraline,	m, Fluoxetine, Fluvoxamine, Venlafaxine	, Nefazodone,	
Serotonin Reuptake Inhibitors-class	Clozapine, see <i>Sedative/Hypno</i> Serotonin Reuptake Inhibitors	otics/Agents used in Psychiatry (An	tipsychotic Agents)—	

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT		
	Cyclosporine	Increased concentrations of cyclosporine.	Monitor cyclosporine concentrations. Decrease cyclosporine dose if necessary.		
	Cyproheptadine	Decreased antidepressant effects of serotonin reuptake inhibitor.	Discontinue cyproheptadine if necessary.		
	MAO Inhibitors [isocarboxazid, phenelzine, selegiline, tranylcypromine]	Increased risk of serotonin syndrome (CNS irritability, shivering, myoclonus, altered consciousness).	Avoid combination. Allow at least 2 weeks after stopping MAO inhibitor before starting serotonin reuptake inhibitor, and vice versa. Allow at least 5 weeks after stopping fluoxetine before starting MAO inhibitor.		
	Sibutramine, see Miscellaneo	us Agents			
	Sympathomimetics [amphetamine, benzphetamine, dextroamphetamine, dexfenfluramine, diethylpropion, fenfluramine, mazindol, methamphetamine, phendimetrazine, phenmetrazine, phentermine]	Increased risk of serotonin syndrome (CNS irritability, shivering, myoclonus, altered consciousness).	Avoid combination if possible. Otherwise, monitor for signs/symptoms of CNS toxicity and adjust dose of one or both drugs as needed.		
	Tricyclic Antidepressants, see Serotonin Reuptake Inhibitors	Sedatives/Hypnotics/Agents used	in Psychiatry (Antidepressants)-		
Fluoxetine (see also Serotonin Reuptake Inhibitors-class)	Carbamazepine, see Anticonv	ulsants			
	Phenytoin, see Anticonvulsan	ts (Hydantoins)			
	Thioridazine, see Sedatives/Hypnotics/Agents used in Psychiatry (Antipsychotic Agents)				
Fluvoxamine (see also Serotonin Reuptake Inhibitors-class)	Methadone, see Pain Medica	tions (Narcotic)-Protease Inhibitors			
	Tacrine	Increased concentrations of tacrine.	Avoid combination if possible. Otherwise, monitor liver function tests. Use alternative serotonin reuptake inhibitor (eg, fluoxetine).		
	Thioridazine, see Sedatives/Hypnotics/Agents used in Psychiatry (Antipsychotic Agents)				
Paroxetine (see also Serotonin Reuptake Inhibitors-class)	Desipramine, see Sedatives/H (Tricyclic Antidepressants)	ypnotics/Agents used in Psychiatry,	Antidepressants		
	Imipramine, see Sedatives/Hypnotics/Agents used in Psychiatry, Antidepressants (Tricyclic Antidepressants)				
	Phenothiazines, see Sedatives	s/Hypnotics/Agents used in Psychia	try (Antipsychotic Agents)		
Sertraline (see also Serotonin Reuptake Inhibitors-class)	Phenytoin, see Anticonvulsan	ts (Hydantoins)			

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
Tricyclic		ne, Clomipramine, Desipram	
Antidepressants (TCAs)	Imipramine, Nortriptylin	ne, Protriptyline, Trimipramii	ne
, ,			
Tricyclic Antidepressants-class	Carbamazepine, see Anticonv	ulsants	
	Cimetidine	Increased concentrations of tricyclic antidepressant.	Monitor tricyclic antidpressant concentrations. Adjust tricyclic antidepressant dose as needed when starting or stopping cimetidine. Use alternative histamine H <sub>2</sub> -antagonist (eg, ranitidine).
	Clonidine, see Antihypertensiv	ve and Cardiovascular Agents, Adrei	nergic Modifiers
	Serotonin Reuptake Inhibitors (fluoxetine, fluvoxamine, paroxetine, sertraline)	Increased concentrations of tricyclic antidepressant. Increased risk of serotonin syndrome (CNS irritability, shivering, myoclonus, altered consciousness).	Monitor tricyclic antidepressant concentra- tions and for signs/symptoms of toxicity. Decrease tricyclic antidepressant dose if necessary.
	MAO Inhibitors [phenelzine, tranylcypromine]	Hyperpyretic crisis, seizures. May progress to death.	Avoid combination. Do not administer tricyclic antidepressant within 2 weeks of MAO inhibitor therapy.
	Rifamycins [rifabutin, rifampin]	Decreased concentrations of tricyclic antidepressant.	Monitor tricyclic antidepressant concentra- tions. Increase tricyclic antidepressant dose if necessary.
	Sparfloxacin	Increased risk of cardiac arrhythmias, including torsades de pointes.	Avoid combination. Use alternative quinolones (eg, ciprofloxacin, levofloxacin).
	Sympathomimetics [dobutamine, dopamine, ephedrine, epinephrine, mephentermine, metaraminol, methoxamine, norepinephrine, phenylephrine]	Increased pressor effects of direct-acting sympathomimetics. Decreased pressor effects of indirect-acting sympathomimetics.	Monitor for hypertension and dysrrhythmias. Adjust sympathomimetic dose as needed.
	Valproic Acid [divalproex, valproate sodium, valproic acid]	Increased concentrations of tricyclic antidepressant. Increased risk of serotonin syndrome (CNS irritability, shivering, myoclonus, altered consciousness).	Monitor tricyclic antidepressant concentra- tions and for signs/symptoms of toxicity. Decrease tricyclic antidepressant dose if necessary.
Miscellaneous Antido	epressants		
Bupropion	Carbamazepine	Decreased effects of bupropion.	Increase bupropion dose if necessary.
	MAO Inhibitors [phenelzine, tranylcypromine]	Increased risk of acute bupropion toxicity (seizures).	Avoid combination. Allow at least 2 weeks after stopping MA0 inhibitor before starting bupropion.

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
	Ritonavir	Increased risk of bupropion toxicity.	Avoid combination.
Lithium	Angiotensing Converting Enzyme Inhibitors [benazepril, captopril, enalapril, fosinopril, lisinopril, moexipril, quinapril, ramipril, trandolapril]	Increased concentrations of lithium.	Monitor lithium concentrations and for signs/symptoms of toxicity.
	Angiotensin II Receptor Blockers [candesartan, eprosartan, irbesartan, losartan, olmesartan, telmisartan, valsartan]	Increased concentrations of lithium.	Monitor lithium concentrations and for signs/symptoms of toxicity.
	Carbamazepine	Increased risk of neurotoxicity (lethargy, muscular weakness, ataxia, tremor, hyperreflexia).	Monitor for signs/symptoms of toxicity. Discontine one or both drugs if necessary.
	Haloperidol, see Sedatives/Hy	pnotics/Agents used in Psychiatry	(Antipsychotic Agents)
	lodide Salts [calcium iodide, hydrogen iodide, iodide, iodinated glycerol, iodine, potassium iodide, sodium iodide]	Increased risk of hypothyroidism.	Avoid combination if possible Otherwise, adminsiter thyroid hormone if necessary
	NSAIDs [diclofenac, ibuprofen, indomethacin, ketorolac, meloxicam, naproxen, piroxicam, sulindac]	Increased concentrations of lithium.	Monitor lithium concentrations. Adjust lithium dose as needed when starting or stopping NSAID.
	Sibutramine, see Miscellaneou	us Agents	
	Thiazide Diuretics [bendroflumethiazide, benzthiazide, chlorothiazide, chlorthalidone, hydrochlorothiazide, hydroflumethiazide, indapamide, meloxicam, methyclothiazide, quinethazone, sulindac, trichlormethiazide]	Increased concentrations of lithium.	Monitor lithium concentrations. Decrease lithium dose if necessary.
	Urinary Alkalinizers [potassium citrate, sodium acetate, sodium bicarbonate, sodium citrate, sodium lactate, tromethamine]	Decreased concentrations of lithium.	Avoid combination.
<b>ANTIPSYCHOT</b>			
Clozapine	Ritonavir	Increased concentrations of clozapine.	Avoid combination.
	Serotonin Reuptake Inhibitors [fluoxetine, fluvoxamine, sertraline]	Increased concentrations of clozapine.	Monitor clozapine concentrations. Decrease clozapine dose if necessary.

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT		
Haloperidol	Anticholinergics [atropine, belladonna, benztropine, biperiden, clidinium, dicyclomine, glycopyrrolate, hyoscyamine, mepenzolate, methscopolamine, orphenadrine, oxybutynin, procyclidine, propantheline, scopolamine, trihexyphenidyl]	Decreased concentrations of haloperidol. Worsening of schizophrenic symptoms. Development of tardive dyskinesia.	Discontinue anticholinergic or increase haloperidol dose if necessary.		
	Azole Antifungals [fluconazole, itraconazole, ketoconazole]	Increased concentrations of haloperidol.	Adjust haloperidol dose as needed when starting or stopping azole antifungal.		
	Carbamazepine	Decreased effects of haloperidol. Increased effects of carbamazepine.	Adjust dose of one or both drugs as needed.		
	Lithium	Alterations in consciousness, encephalopathy, extrapyramidal effects, fever, leukocytosis, and increased serum enzymes.	Avoid combination if possible. Otherwise, discontinue one or both drugs and provide supportive treatment if necessary.		
	Rifamycins [rifabutin, rifampin]	Decreased effects of haloperidol.	Adjust haloperidol dose as needed when starting or stopping rifamycin.		
Phenothiazines	Methotrimeprazine, Per	romazine, Fluphenazine, Me phenazine, Prochlorperazin azine, Thiethylperazine, Thio omazine	e, Promazine,		
Phenothiazines-class	Anticholinergics [atropine, belladonna, benztropine, biperiden, clidinium, dicyclomine, glycopyrrolate, hyoscyamine, isopropamide, mepenzolate, orphenadrine, oxybutynin, oxyphencyclimine, procyclidine, propantheline, scopolamine, trihexyphenidyl]	Decreased effects of phenothiazine.	Increase phenothiazine dose if necessary.		
	Ethanol, see Miscellaneous Agents				
	Paroxetine	Increased effects of phenothiazine. Increased risk of life-threatening cardiac arrhythmias with thioridazine.	Avoid combination if possible (thioridazine is contraindicated). Adjust phenothiazine dose as needed.		
	Propranolol, see Antihypertensive and Cardiovascular Agents (Beta-Blockers)				
	Sparfloxacin	Increased risk of cardiac arrhythmias, including torsades de pointes.	Avoid combination. Use alternative quinolones (eg, ciprofloxacin, levofloxacin).		
<b>Chlorpromazine</b> (see also Phenothiazines-class)	Meperidine, see Pain Medicat	ions (Narcotic)—Phenothiazines			
<b>Propiomazine</b> (see also Phenothiazines-class)	Meperidine, see Pain Medicat	ions (Narcotic)—Phenothiazines			

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT		
<b>Thioridazine</b> (see also Phenothiazines-class)	Antiarrhythmic Agents [amiodarone, bretylium, disopyramide, procainamide, quinidine, sotalol]	Increased risk of cardiac arrhythmias, including torsades de pointes.	Avoid combination.		
	Fluoxetine	Increased risk of cardiac arrhythmias, including torsades de pointes.	Avoid combination.		
	Fluvoxamine	Increased risk of cardiac arrhythmias, including torsades de pointes.	Avoid combination.		
	Pimozide	Increased risk of cardiac arrhythmias, including torsades de pointes.	Avoid combination.		
SEDATIVES					
Barbiturates		tal, Butabarbital, Butalbital, rbital, Primidone, Secobarb			
Barbiturates-class	Beta-Blockers, see Antihypert (Cardio-Selective and Noncard	rensive and Cardiovascular Agents dio-Selective Beta-Blockers)			
	Corticosteroids, see Corticoste	eroids			
	Doxycycline, see Antimicrobia	l Agents (Antibacterial Antibiotics -	Tetracyclines)		
	Estrogens, see Miscellaneous Agents				
	Ethanol, see Miscellaneous Agents				
	Felodipine, see Antihypertensive and Cardiovascular Agents (Calcium Channel-Blockers)				
	Griseofulvin, see Antimicrobial Agents (Miscellaneous Antifungals)—Barbiturates				
	Methadone, see Pain Medications (Narcotic)				
	Metronidazole, see Antimicrobial Agents (Miscellaneous Antibacterial Antibiotics)				
	Nifedipine, see Antihypertensive and Cardiovascular Agents (Calcium-Channel Blockers)				
	Quinidine, see Antihypertensiv	re and Cardiovascular Agents (Antia	arrhythmic Agents)		
	Rifamycins [rifabutin, rifampin]	, see Antimicrobial Agents (Antimy	cobacterial Agents)		
	Theophyllines, see <i>Bronchodil</i>	ators			
	Voriconazole, see Antimicrobi	al Agents (Azole Antifungals)—Bart	biturates		
	Warfarin, see Anticoagulants/	Thrombolytics			
Benzodiazepines		poxide, Clonazepam, Cloraz Halazepam, Lorazepam, Mi , Triazolam			
Benzodiazepines, Oxidative Metabolism-class [alprazolam, chlordiazepoxide, clonazepam, clorazepate, diazepam, estazolam, flurazepam, halazepam, midazolam, quazepam, triazolam]	Azole Antifungals [fluconazole, itraconazole, ketoconazole, miconazole, voriconazole]	Increased concentrations of benzodiazepine. Prolonged CNS depression and psychomotor impairment.	Avoid combination if possible (alprazolam and triazolam are contraindicated with itraconazole and ketoconazole). Otherwise, decrease benzodiazepine dose.		
	Diltiazem	Increased effects of benzodiazepine (diazepam, midazolam, triazolam). Prolonged sedation and respiratory depression.	Decrease benzodiazepine dose.		

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
	Ethanol, see Miscellaneous A	Agents	
	Grapefruit Juice	Increased effects of benzodiazepine. Delayed onset of benzodiazepine effects.	Avoid combination.
	Macrolide Antibiotics [clarithromycin, erythromycin, troleandomycin]	Increased concentrations of benzodiazepine. Prolonged sedation and respiratory depression.	Decrease benzodiazepine dose if necessary. Use alternative benzodiazepine (eg, lorazepam, oxazepam, temazepam). Use alternative macrolide antibiotic (eg, azithromycin).
	Protease Inhibitors [indinavir, ritonavir, saquinavir]	Increased concentrations of benzodiazepine. Prolonged sedation and respiratory depression.	Avoid combination. Use alternative benzodiazepine (eg, lorazepam, oxazepam, temazepam).
	Ritonavir	Prolonged sedation and respiratory depression.	Substitute lorazepam, oxazepam, or temazepam.
Miscellaneous Sed	atives		
Buspirone	Azole Antifungals [fluconazole, itraconazole, ketoconazole, miconazole, voriconazole]	Increased effects of buspirone.	Adjust buspirone dose as needed when starting, stopping, or changing dose of azole antifungal.
	Macrolide Antibiotics [clarithromycin, erythromycin, troleandomycin]	Increased effects of buspirone.	Adjust buspirone dose as needed when starting, stopping, or changing dose of macrolide antibiotic. Use alternative antibiotic if possible.
	Rifamycins [rifabutin, rifampin]	Decreased effects of buspirone.	Adjust buspirone dose as needed when starting, stopping, or changing dose of rifamycin.
Zolpidem	Ritonavir	Severe sedation and respiratory depression.	Avoid combination.
TRANSPLANT II	MMUNOSUPPRESSA.	NTS	
Cyclosporine	Amiodarone	Increased concentrations of cyclosporine.	Monitor cyclosporine concentrations and for signs/symptoms of toxicity. Decrease cyclosporine dose if necessary.
	Androgens (danazol, methyltestosterone)	Increased concentrations of cyclosporine.	Monitor cyclosporine concentrations and for signs/symptoms of toxicity. Decrease cyclosporine dose if necessary.
	Azole Antifungals [fluconazole, itraconazole, ketoconazole]	Increased concentrations of cyclosporine.	Monitor cyclosporine concentrations and for signs/symptoms of toxicity. Adjust cyclosporine dose as needed when starting or stopping azole antifungal.
	Carbamazepine	Decreased concentrations of cyclosporine.	Monitor cyclosporine concentrations and for signs/symptoms of organ rejection. Increase cyclosporine dose if necessary.

DRUG

Caspofungin  Increased concentrations of caspofungin. Elevated liver function test results.  Increased risk of cyclosporine dose if necessary.  Colchicine  Increased risk of cyclosporine toxicity (GI, hepatic, renal, neuromuscular).  Digoxin, see Antihypertensive and Cardiovascular Agents (Miscellaneous Antihypertensive and Cardiovascular Agents)  Diltiazem  Increased concentrations of cyclosporine.  Increased CNS adverse effects of both drugs (confusion, agitation, tremor).  Lovastatin, see Hypolipidemic Agents (HMG-CoA Reductase Inhibitors)  Increased Concentrations of cyclosporine.  Increased concentrations of cyclosporine difineressary.  Macrolide Antibiotics agitation, tremor).  Lovastatin, see Hypolipidemic Agents (HMG-CoA Reductase Inhibitors)  Increased concentrations of cyclosporine.	EMENT	MANAGEME	POTENTIAL EFFECT	INTERACTING DRUG
of caspofungin. Elevated liver function test results.  Otherwise, more signs/symptom hepatotoxicty. caspofungin if toxicity (GI, hepatic, renal, neuromuscular).  Digoxin, see Antihypertensive and Cardiovascular Agents (Miscellaneous Antihypertensive and Cardiovascular Agents)  Ditiazem  Increased concentrations of cyclosporine.  Increased concentrations of cyclosporine.  Etoposide  Increased concentrations of etoposide.  Increased concentrations of etoposide.  Increased concentrations of cyclosporine.  Foscarnet, see Antimicrobial Agents (Antiviral Agents)  Grapefruit Juice  Increased concentrations of cyclosporine.  Foscarnet, see Antimicrobial Agents (Antiviral Agents)  Grapefruit Juice  Increased concentrations of cyclosporine.  Poercase despit in ecessary.  Foscarnet, see Hypolipidemic Agents (Antiviral Agents)  Increased CNS adverse effects of both drugs (confusion, agitation, tremor).  Lovastatin, see Hypolipidemic Agents (HMG-CoA Reductase Inhibitors)  Macrolide Antibiotics (agithromycin, clarithromycin, clarithromycin, erythromycin, erythromycin, erythromycin, clarithromycin, erythromycin,	s and for ns of toxicity.	Monitor cyclosporin concentrations and signs/symptoms of to Decrease cyclospor if necessary.		Carvedilol
toxicity (GI, hepatic, renal, neuromuscular).  Digoxin, see Antihypertensive and Cardiovascular Agents (Miscellaneous Antihypertensive and Cardiovascular Agents)  Diltiazem  Increased concentrations of cyclosporine.  Etoposide  Increased concentrations of etoposide.  Increased concentrations of etoposide.  Etoposide  Increased concentrations of etoposide.  Monitor cyclos concentrations of etoposide.  Foscarnet, see Antimicrobial Agents (Antiviral Agents)  Grapefruit Juice  Increased concentrations of cyclosporine.  Decreased concentrations of cyclosporine.  Decreased concentrations of cyclosporine.  Decreased concentrations of cyclosporine.  Imipenem/Cilastatin  Increased CNS adverse effects of both drugs (confusion, agitation, tremor).  Lovastatin, see Hypolipidemic Agents (HMG-CoA Reductase Inhibitors)  Macrolide Antibiotics lazithromycin, clarithromycin, erythromycin, erythr	nitor for ns of Discontinue	Avoid combination if Otherwise, monitor f signs/symptoms of hepatotoxicty. Disco caspofungin if neces	of caspofungin. Elevated liver	Caspofungin
Increased concentrations of cyclosporine.  Etoposide Increased concentrations of etoposide.  Increased concentrations of etoposide.  Increased concentrations of etoposide.  Etoposide Increased concentrations of etoposide.  Foscarnet, see Antimicrobial Agents (Antiviral Agents)  Grapefruit Juice Increased concentrations of cyclosporine.  Hydantoins [ethotoin, fosphenytoin, mephenytoin, phenytoin]  Increased CNS adverse effects of both drugs (confusion, agitation, tremor).  Lovastatin, see Hypolipidemic Agents (HMG-CoA Reductase Inhibitors)  Macrolide Antibiotics [azithromycin, clarithromycin, erythromycin, troleandomycin]  Metoclopramide Increased concentrations of cyclosporine.  Monitor cyclos concentrations of cyclosporine.	s and for ns of toxicity. losporine	Monitor cyclosporin concentrations and signs/symptoms of to Decrease cyclospor dose if necessary.	toxicity (GI, hepatic, renal,	Colchicine
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of metoclopran	s and for ns of toxicity. corine dose en starting, nanging dose	Monitor cyclosporin concentrations and signs/symptoms of to Adjust cyclosporine as needed when sta stopping, or changin of metoclopramide.		Metoclopramide

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT		
	Nefazodone	Increased concentrations of cyclosporine.	Monitor cyclosporine concentrations and for signs/symptoms of toxicity. Decrease cyclosporine dose if necessary.		
	Nicardipine	Increased concentrations of cyclosporine.	Monitor cyclosporine concentrations and for signs/symptoms of toxicity. Decrease cyclosporine dose if necessary.		
	Orlistat	Increased concentrations of cyclosporine.	Avoid combination.		
	Probucol	Decreased concentrations of cyclosporine.	Monitor cyclosporine concentrations and for signs/ symptoms of organ rejection. Increase cyclosporine dose if necessary.		
	Quinolones [ciprofloxacin, norfloxacin]	Increased risk of nephrotoxicity.	Monitor cyclosporine concentrations and for signs/symptoms of toxicity. Use alternative quinolone (eg, levofloxacin).		
	Rifamycins [rifabutin, rifampin]	Decreased concentrations of cyclosporine.	Avoid combination if possible. Otherwise, monitor cyclosporine concentrations and for signs/symptoms of organ rejection. Adjust cyclosporine dose as needed when starting, stopping, or changing dose of rifamycin.		
	Serotonin Reuptake Inhibitors, see Sedatives/Hypnotics/Agents used in Psychiatry (Antidepressants)				
	Sirolimus, see Transplant Immunosuppressants				
	Sulfonamides [sulfadiazine, sulfamethoxazole, trimethoprim/ sulfamethoxazole]	Decreased effects of cyclosporine. Increased risk of nephrotoxicity with oral sulfonamides.	Avoid combination if possible. Otherwise, monitor cyclosporine concentrations and for signs/symptoms of organ rejection. Adjust cyclosporine dose as needed when starting, stopping, or changing dose of sulfonamide.		
	Terbinafine	Decreased concentrations of cyclosporine.	Monitor cyclosporine concentrations and for signs/ symptoms of organ rejection. Adjust cyclosporine dose as needed when starting or stopping terbinafine.		
	Verapamil	Increased concentrations of cyclosporine. Possible nephroprotective effect if verapamil is adminstered before cyclosporine.	Monitor cyclosporine concentrations and for signs/symptoms of toxicity. Decrease cyclosporine dose if necessary.		
Mycophenolate mofetil	Iron Salts, Oral [ferrous fumarate, ferrous gluconate, ferrous sulfate, iron polysaccharide]	Decreased effects of mycophenolate.	Separate administration times. Monitor clinical response and increase mycophenolate dose if necessary.		

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
	Tacrolimus	Increased concentrations of mycophenolate.	Monitor mycophenolic acid levels. Adjust mycophenolate doses as needed when starting or stopping tacrolimus.
Sirolimus	Azole Antifungals [fluconazole, itraconazole, ketoconazole, voriconazole]	Increased concentrations of sirolimus.	Monitor sirolimus concentrations and for signs/symptoms of toxicity. Adjust sirolimus dose as needed when starting or stopping azole antifungal.
	Cyclosporine	Increased concentrations of sirolimus.	Administer sirolimus 4 hours after cyclosporine to prevent changes in sirolimus concentrations.
	Diltiazem	Increased concentrations of sirolimus.	Monitor sirolimus concentrations and for signs/symptoms of toxicity. Adjust sirolimus dose as needed when starting or stopping diltiazem.
Tacrolimus	Azole Antifungals [fluconazole, itraconazole, ketoconazole, miconazole, voriconazole]	Increased concentrations of tacrolimus.	Monitor tacrolimus concentrations and for signs/symptoms of toxicity. Adjust tacrolimus dose as needed when starting or stopping azole antifungal.
	Caspofungin	Decreased concentrations of tacrolimus.	Monitor tacrolimus concentrations. Adjust tacrolimus dose as needed when starting or stopping caspofungin.
	Diltiazem	Increased concentrations of tacrolimus.	Monitor tacrolimus concentrations and for signs/symptoms of toxicity. Decrease tacrolimus dose if necessary.
	Hydantoins [fosphenytoin, phenytoin]	Decreased concentrations of tacrolimus. Increased concentrations of phenytoin.	Monitor tacrolimus and phenytoin concentrations. Adjust doses of one or both drugs as needed.
	Macrolide Antibiotics [clarithromycin, erythromycin, troleandomycin]	Increased concentrations of tacrolimus.	Monitor tacrolimus concentrations and for signs/symptoms of toxicity. Adjust tacrolimus dose as needed when starting or stopping azole antifungal. Use alternative antibiotic.
	Mycophenolate mofetil, see 7	ransplant Immunosuppressants	
	Nifedipine	Increased concentrations of tacrolimus.	Monitor tacrolimus concentrations and for signs/symptoms of toxicity. Decrease tacrolimus dose if necessary.

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
	Rifamycins [rifabutin, rifampin, rifapentine]	Decreased concentrations of tacrolimus.	Monitor tacrolimus concentrations. Adjust tacrolimus dose as needed when starting or stopping rifamycin.
VITAMINS			
Folic acid	Phenytoin, see Anticonvulsant	ts	
Vitamin E (Tocopherol)	Warfarin, see Anticoagulants/	Thrombolytic Agents	
Vitamin K (Phytonadione)	Warfarin, see Anticoagulants/	Thrombolytic Agents	
<b>MISCELLANEOUS</b>	AGENTS		
Ergot Alkaloids [dihydroergotamine, ergotamine, methysergide}	Beta-Blockers [carteolol, nadolol, penbutolol, pindolol, propranolol, timolol]	Increased risk of ergot toxicity (peripheral ischemia, gangrene).	Discontinue beta-blocker or decrease ergot alkaloid dose if necessary.
	Macrolide Antibiotics [clarithromycin, erythromycin, troleandomycin]	Acute ergotism (peripheral ischemia).	Avoid combination if possible. Use alternative antibiotic. Discontinue one or both drugs if ergotism develops. Administer sodium introprusside to decrease macrolide-ergot induced vasopasm if necessary.
	Nitrates [amyl nitrite, isosorbide dinitrate, nitroglycerin]	Increased standing systolic blood pressure. Pharmacologic antagonism between dihydroergotamine and nitroglycerin may decrease antianginal effects of nitroglycerin.	Decrease dihydroergotamine dose if necessary.
	NNRT Inhibitors [delavirdine, efavirenz]	Increased risk of ergot toxicity (peripheral ischemia, peripheral vasospasm).	Avoid combination.
	Protease Inhibitors [amprenavir, indinavir, nelfinavir, ritonavir, saquinavir]	Increased risk of ergot toxicity (peripheral ischemia, peripheral vasospasm).	Avoid combination.
	Sibutramine, see Miscellaneo	us Agents	
	Voriconazole	Increased risk of ergot toxicity (peripheral ischemia, peripheral vasospasm).	Avoid combination.
Estrogens [chlorotrianisene, conjugated estrogens, diethylstilbesterol, esterified estrogens, estradiol, estriol, estrogenic substance, estrone, estropipate, ethinyl estradiol, mestranol, quinestrol]	Barbiturates [amobarbital, aprobarbital, butabarbital, butalbital, mephobarbital, pentobarbital, phenobarbital, primidone, secobarbital, thiamylal]	Decreased concentrations of estrogen.	Use alternative nonhormonal or additional method of contraception. Increase estrogen dose if necessary.
	Hydrocortisone, see <i>Corticost</i>	eroids	
	Hydantoins [ethotoin, fosphenytoin, mephenytoin, phenytoin]	Decreased concentrations of estrogen. Possible loss of seizure control.	Use alternative nonhormonal or additional method of contraception. Increase estrogen dose if necessary.

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT		
	Methylprednisolone, see Cort	icosteroids			
	Prednisolone and Prednisone,				
	Rifamycins [rifabutin, rifampin, rifapentine]	Decreased concentrations of estrogen	Use alternative nonhormonal or additional method of contraception. Increase estrogen dose if necessary.		
thanol	Acetaminophen, see Pain Me				
	Alfentanil	Increased tolerance to alfentanil with chronic ethanol ingestion.	Increase alfentanil dose if necessary.		
	Barbiturates [amobarbital, butabarbital, butalbital, mephobarbital, pentobarbital, phenobarbital, primidone, secobarbital]	Additive CNS effects with acute ethanol ingestion (potentially fatal).	Avoid combination.		
	Benzodiazepines [alprazolam, chlordiazepoxide, clorazepate, diazepam, estazolam, flurazepam, halazepam, lorazepam, midazolam, oxazepam, prazepam, quazepam, temazepam, triazolam]	Additive CNS effects with acute ethanol ingestion.	Avoid combination.		
	Cephalosporins [cefamandole, cefoperazone, ceforanide, cefonicid, cefotetan moxalactam]	Disulfuram-like reaction.	Avoid combination.		
	Chloral Hydrate	Additive CNS depression. Disulfiram-like reaction.	Avoid combination.		
	Chlorpropamide, see <i>Hypogly</i>				
	Disulfiram	Flushing, tachycardia, bronchospasm, sweating, nausea, and vomiting. May progress to death.	Avoid combination.		
	Furazolindone	Disulfiram-like reaction.	Avoid combination.		
	Glutethimide	Additive CNS depression.	Avoid combination.		
	Insulin, see Hypoglycemic Agents				
	Levothyroxine, see Miscellaneous Agents				
	Meprobamate	Increased CNS depression.	Avoid combination.		
	Metronidazole	Disulfiram-like reaction.	Avoid combination.		
	Phenothiazines [acetophenazine, chlorpromazine, fluphenazine, mesoridazine, perphenazine, prochlorperazine, promazine, promethazine, thioridazine, trifluoperazine, triflupromazine, trimeprazine]	Increased CNS depression and psychomotor impairment.	Avoid combination.		

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT		
	Sulfonylureas [acetohexamide, chlorpropamide, glipizide, glyburide, tolazamide, tolbutamide]	Prolonged hypoglycemia. Disulfiram-like reaction when taken with chlorpropamide.	Avoid combination.		
	Verapamil	Increased and prolonged CNS depression and psychomotor impairment.	Limit ethanol ingestion.		
Levothyroxine	Cholestyramine	Decreased GI absorption of levothyroxine.	Separate administration times by at least 6 hours. Monitor thyroid function. Increase levothyroxine dose if necessary.		
	Estrogens [conjugated estrogens, esterified estrogens, estradiol, estrone, estropipate, esthinyl estradiol, mestranol]	Decreased serum concentrations of free thyroxine. Increased serum concentrations of thyrotropin.	Monitor serum thyrotropin concentrations approximately 12 weeks after starting estrogen. Adjust levothyroxine dose as needed.		
	Iron Salts (Oral) [ferrous fumarate, ferrous gluconate, ferrous sulfate, iron polysaccharide]	Decreased GI absorption of levothyroxine.	Separate administration times. Monitor thyroid function. Increase levothyroxine dose if necessary.		
	Sucralfate	Decreased GI absorption of levothyroxine.	Separate administration times by at least 8 hours. Monitor thyroid function. Increase levothyroxine dose if necessary.		
	Theophylline, see Bronchodilators (Theophyllines)—Thyroid Hormones				
	Warfarin, see Anticoagulants/Thrombolytic Agents—Thyroid Hormones				
Metyrapone	Cyproheptadine	Decreased pituitary-adrenal response to metyrapone.	Discontinue cyproheptadine before testing pituitary-adrenal axis with metyrapone.		
	Hydantoins [ethotoin, fosphenytoin, mephenytoin, phenytoin]	Decreased pituitary-adrenal response to metyrapone.	Consider doubling metyrapone dose when testing pituitary-adrenal axis function in patients on chronic hydantoin therapy.		
Quinine	Digoxin, see Antihypertensive and Cardiovascular Agents (Miscellaneous Antihypertensive and Cardiovascular Agents)				
	Rifamycins [rifabutin, rifampin, rifapentine]	Decreased concentrations of quinine.	Monitor ECG and quinine concentrations. Increase quinine dose if necessary.		
	Warfarin, see Anticoagulants/Thrombolytic Agents				
Sibutramine	Dextromethorphan	Increased risk of serotonin syndrome (CNS irritability, shivering, myoclonus, altered consciousness).	Avoid combination if possible. Otherwise, obtain medical treatment if serotonin syndrome develops.		
	Ergot Alkaloids	Increased risk of serotonin syndrome (CNS irritability, shivering, myoclonus, altered consciousness).	Avoid combination if possible. Otherwise, obtain medical treatment if serotonin syndrome develops.		

DRUG	INTERACTING DRUG	POTENTIAL EFFECT	MANAGEMENT
	Lithium	Increased risk of serotonin syndrome (CNS irritability, shivering, myoclonus, altered consciousness).	Avoid combination if possible Otherwise, obtain medical treatment if serotonin syndrome develops.
	MAO Inhibitors [isocarboxazid, phenelzine, tranylcypromine]	Increased risk of serotonin syndrome (CNS irritability, shivering, myoclonus, altered consciousness).	Avoid combination. Allow at least 2 weeks after stopping MAO inhibitor before starting sibutramine, and vice versa.
	Meperidine	Increased risk of serotonin syndrome (CNS irritability, shivering, myoclonus, altered consciousness).	Avoid combination if possible Otherwise, obtain medical treatment if serotonin syndrome develops.
	Selective 5HT-1 Receptor Antagonists [almotriptan, naratriptan, rizatriptan, sumatriptan, zolmitriptan]	Increased risk of serotonin syndrome (CNS irritability, shivering, myoclonus, altered consciousness).	Avoid combination if possible Otherwise, obtain medical treatment if serotonin syndrome develops.
	Serotonin Reuptake Inhibitors [fluoxetine, fluvoxamine, nefazodone, paroxetine, sertraline, venlafaxine]	Increased risk of serotonin syndrome (CNS irritability, shivering, myoclonus, altered consciousness).	Avoid combination if possible Otherwise, obtain medical treatment if serotonin syndrome develops.
	Tryptophan	Increased risk of serotonin syndrome (CNS irritability, shivering, myoclonus, altered consciousness).	Avoid combination if possible Otherwise, obtain medical treatment if serotonin syndrome develops.

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